FORM PTO-1390 (REV 11-98) U.S. DEPARTMENT OF COMMERCE PATENT AND TRADEMARK OFFICE

TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY'S DOCKET NUMBER: 146.1374

U.S. APPLICATION NO. (If known, see 37 CFR 1.5): 09/980054

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	PRIORITY DATE CLAIMED
PCT/FR00/01567	June 8, 2000	June 9, 1999

TITLE OF INVENTION: NOVEL CANDIDA ALBICANS GENES AND PROTEINS CODED BY THESE GENES

APPLICANT(S) FOR DO/EO/US: LALANNE et al

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. [X] This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. [ ] This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. [X] This express request to begin national examination procedures (35 U.S.C. 371(f)) at any time rather than delay examination until the expiration of the applicable time limit set in 35 U.S.C. 371(b) and PCT Articles 22 and 39(1).
4. [ ] A proper Demand for International Preliminary Examination was made by the 19th month from the earliest claimed priority date.
5. [X] A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. [X] is transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] has been transmitted by the International Bureau.
   c. [ ] is not required, as the application was filed in the United States Receiving Office (RO/US).
6. [X] A translation of the International Application into English (35 U.S.C. 371(c)(2)).
7. [ ] Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. [ ] are transmitted herewith (required only if not transmitted by the International Bureau).
   b. [ ] have been transmitted by the International Bureau.
   c. [ ] have not been made; however, the time limit for making such amendments has NOT expired.
   d. [ ] have not been made and will not be made.
8. [ ] A translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. [X] An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)). Unexecuted
10. [ ] A translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. [X] An Information Disclosure Statement under 37 CFR 1.97 and 1.98. (two)
12. [ ] An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. [X] A FIRST preliminary amendment.
    [ ] A SECOND or SUBSEQUENT preliminary amendment.
14. [ ] A substitute specification.
15. [ ] A change of power of attorney and/or address letter.
16. [X] Other items or information: International Preliminary Examination Report; PCT/ISA/220; PCT/IB/306 ; Paper Copy of Sequence Listing (within application); Diskette of Sequence Listing

U.S. APPLICATION NO. (if known, see 37 CFR 1.5)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
09/980054	PCT/FR00/01567	146.1374

	CALCULATIONS PTO USE ONLY	
17. [X] The following fees are submitted:		
BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)) :	$1040.00	
Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2)) paid to USPTO and International Search Report not prepared by the EPO or JPO **$970.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO **$840.00**		
International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2)) paid to USPTO **$760.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33(1)-(4) **$670.00**		
International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1)-(4) **$96.00**		
ENTER APPROPRIATE BASIC FEE AMOUNT =	$1040.00	
Surcharge of **$130.00** for furnishing the oath or declaration later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(e)).	$	

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE	
Total claims	24 - 20 =	4	X $18.00	$ 72.00
Independent claims	3 - 3 =	0	X $78.00	$ –
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $260.00	$ –

TOTAL OF ABOVE CALCULATIONS =	$ 1112.00	
Reduction of 1/2 for filing by small entity, if applicable. A Small Entity Statement must also by filed (Note 37 CFR 1.9, 1.27, 1.28).	$	
SUBTOTAL =	$ 1112.00	
Processing fee of **$130.00** for furnishing the English translation later than [ ] 20 [ ] 30 months from the earliest claimed priority date (37 CFR 1.492(f)). +	$	
TOTAL NATIONAL FEE =	$ 1112.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property +	$	
TOTAL FEES ENCLOSED =	$ 1112.00	
	Amount to be: refunded	$
	charged	$

a. [xx] ~~A check in the amount of $_____ to cover the above fees is enclosed.~~ PTO Form 2038 For $1112.00 is enclosed.

b. [ ] Please charge my Deposit Account No. _____ in the amount of $_____ to cover the above fees. A duplicate copy of this sheet is enclosed.

c. [X] The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 02-2275. A duplicate copy of this sheet is enclosed.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:
Bierman, Muserlian and Lucas
600 Third Avenue
New York, NY 10016

SIGNATURE:

Charles A. Muserlian
NAME

19,683
REGISTRATION NUMBER

Case No. 146.1374

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s) : Lalanne, J. et al.

Serial No. : 09/980,054 Group Unit : TBA

Filed : November 28, 2001 Examiner : TBA

For : NOVEL GENES OF CANDIDA ALBICANS AND THE PROTEINS CODED BY THESE GENES

Statement Under 37 C.F.R. §1.821(f) or §1.825(b)

Commissioner of Patents
U.S. Patent and Trademark Office
Box Sequence, P.O. Box 2327
Arlington, VA 22202

Dear Sir:

I hereby certify that:

[ ] The paper Sequence Listing submitted herewith and computer readable Sequence Listing attached hereto are identical (37 C.F.R. §1.821(f)).

[X] The substitute paper Sequence Listing and substitute computer readable Sequence Listing submitted herewith are identical. No new matter is included (37 C.F.R. §1.825(b)).

Respectfully submitted,

BIERMAN, MUSERLIAN AND LUCAS, L.L.P.

Date: 4-24-02

By: _____
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684171 v1

Our Ref.: 146.1374

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:
LALANNE et al
PCT/FR00/01567
Serial No.:
Filed: Concurrently Herewith
For: NOVEL *CANDIDA ALBICANS* GENES AND PROTEINS CODED BY THESE GENES

PCT Date: June 8, 2000

600 Third Avenue
New York, NY 10016
November 27, 2001

PRELIMINARY AMENDMENT

Assistant Commissioner for Patents
Washington, D.C. 20231

Sir:

Please amend this application as follows:

IN THE SPECIFICATION:

Page 1, before line 1, insert

--This application is a 371 of PCT/FR00/01567 filed June 8, 2000.--

IN THE CLAIMS:

Claim 1 (amended) An isolated polynucleotide containing a nucleotide sequence selected from the group consisting of

a) a polynucleotide having at least 50% identity with

a polynucleotide coding for a polypeptide having the same function and having an amino acid sequence homologous with a sequence selected from the group consisting of SEQ ID NO: 2, SEQ ID NO: 4, SEQ ID NO: 6, SEQ ID NO: 8, SEQ. ID NO: 10, SEQ. ID NO: 12 and SEQ ID NO: 14,

b) a complementary polynucleotide of polynucleotide a) and

c) a polynucleotide comprising at least 15 consecutive bases of the polynucleotide defined in a) and b).

Claim 2 (amended) A polynucleotide of claim 1 which polynucleotide is of DNA.

Claim 3 (amended) A polynucleotide of claim 1 which polynucleotide is of RNA.

Claim 4 (amended) A polynucleotide of claim 2 comprising a nucleotide sequence selected from the group consisting of SEQ ID. NO: 1, SEQ ID NO: 3, SEQ ID NO: 5, SEQ ID No: 7, SEQ ID No: 9, SEQ ID No.: 11 and SEQ ID No: 13.

Claim 5 (amended) A DNA sequence of claim 1, wherein the DNA sequences are those of the genes coding respectively for the proteins of *Candida albicans* having the same functions as the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 and containing a nucleotide sequence selected

from the group consisting of SEQ ID No: 1, SEQ ID No: 3, SEQ ID No: 5, SEQ ID No.: 7, SEQ ID No: 9, SEQ ID No: 11 and SEQ ID No: 13.

Claim 6 (amended) A DNA sequence of genes of claim 5 coding for an amino acid sequence selected from the group consisting of SEQ ID No: 2, SEQ ID No: 4, SEQ ID No: 6, SEQ ID No: 8, SEQ ID No: 10, SEQ ID No: 12 and SEQ ID No: 14.

Claim 7 (amended) A DNA sequence coding for the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 of claim 5 and the DNA sequence which hybridizes with these and/or have significant homologies with these sequences or the fragments thereof and code for proteins having the same functions.

Claim 8 (amended) A DNA sequence of claim 5 comprising modifications introduced by suppression, insertion and/or substitution of at least one nucleotide coding for the proteins having the same activities as the proteins PCaDR472, PCaDR498, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361.

Claim 9 (amended) A DNA sequence of claim 5 and a DNA sequence which has an homology of nucleotide sequence of at least 50% with said DNA sequences.

Claim 10 (amended) A DNA sequence of claim 5 and a DNA

sequence which codes for the proteins with similar functions, the respective AA sequences of which have an homology of at least 40%, rather at least 60% with the AA sequences coded by said DNA sequence.

Claim 11 (amended) A polypeptide having an amino acid sequence selected from the group consisting of SEQ ID No: 2, SEQ ID No: 4, SEQ ID No: 6, SEQ ID No.: 8, SEQ ID No: 10, SEQ ID No: 12 and SEQ ID No.: 14 coded by the DNA sequence of claim 5 and the analogs of the polypeptide.

Claim 12 (amended) A polypeptide of recombinant proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 having respectively the amino acid sequences SEQ ID No: 2, SEQ ID No: 4, SEQ ID No: 6, SEQ ID No 8, SEQ ID No: 10, SEQ ID No: 12 and SEQ ID No: 14 comprising, for the preparation of each of the proteins, expressing in an appropriate host the DNA sequence coding for the protein of claim 5 and isolating and purifying said recombinant protein.

Claim 13 (amended) An expression vector containing one of the DNA sequences of claim 5.

Claim 14 (amended) A host cell transformed with a vector of claim 13.

Claim 15 (amended) The process of claim 12 wherein the host cell is DH5 alpha E. coli or XL1-Blue E. coli.

Claim 16 (amended) The process of claim 13 wherein the host cell is Saccharomyces cerevisae.

Claim 17 (amended) At least one plasmid deposited at the CNCM under the numbers I-2214, I-2215, I-2216, I-2217, IK-2211, I-2212 and I-2213.

Claim 18 (amended) A screening process for antifungal products comprising a stage where the activity of one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 as defined in claim 11 is measured, in the presence of each of the products of which one wishes to determine the antifungal properties and selecting the products having an inhibitory effect on this activity.

Claim 21 (amended) A pharmaceutical composition containing as active ingredient at least one inhibitor of the proteins of *Candida albicans* of claim 20.

Claim 24 (amended) An antibody directed against a polypeptide of claim 11 or a fragment of this polypeptide having the same function.

Claim 25 (amended) The antibody of claim 24 directed against any one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 or a fragment of these proteins.

Claim 27 (amended) A kit for the diagnosis of fungal infections comprising a DNA sequence of claim 5 or a sequence having a similar function or a functional fragment of this sequence, the polypeptide coded by this sequence or a polypeptide fragment having the same function or an antibody directed against such polypeptide coded by this DNA sequence or against a fragment of this polypeptide.

Cancel claims 19, 20, 22, 23 and 26 and add the following.

--28. A method of inducing an immunological response in a mammal comprising inoculating a mammal in need thereof with a polypeptide of claim 11 to produce an antibody to protect the mammals.

29. A method of treating a disease caused by *Candida albicans* yeast in mammals comprising administering to a mammal in need thereof a gene selected from the group consisting of CaDR472, CaDR489, 1CaDR527, 2CaDR527, CaFL024, CaNL260 and CaDR361 or of any one of the proteins coded by these genes.--

REMARKS

The amendment is being submitted to insert reference to the PCT application, remove multiple dependency from the claims and to conform the claims to the American practice.

Respectfully submitted,
BIERMAN, MUSERLIAN AND LUCAS

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Tel. # (212) 661-8000

CAM:sd
Enclosures: Marked-up Version of Claims
Return Receipt Postcard

MARKED-UP VERSION OF CLAIMS

09/980054

JC13 Rec'd PCT/PTO 28 NOV 2001

1) An isolated polynucleotide ~~each~~ containing a nucleotide sequence ~~chosen~~ selected from the ~~following~~ group consisting of

a) a polynucleotide having at least 50 % ~~or at least 60 % and preferably at least 70 %~~ identity with a polynucleotide coding for a polypeptide having the same function and having an amino acid sequence homologous with a sequence ~~chosen~~ selected from the group consisting of SEQ ID No: 2, SEQ ID No: 4, SEQ ID No: 6, SEQ ID No: 8, SEQ ID No: 10, SEQ ID No: 12 and SEQ ID No: 14,

b) a complementary polynucleotide of polynucleotide a) and

c) a polynucleotide comprising at least 15 consecutive bases of the polynucleotide defined in a) and b).

2) A polynucleotides ~~according to~~ of claim 1 ~~such that these~~ which polynucleotides ~~are~~ is of DNA.

3) A polynucleotides ~~according to~~ of claim 1 ~~such that these~~ which polynucleotides ~~are~~ is of RNA.

4) A polynucleotides ~~as defined in~~ of claim 2 ~~each~~ comprising a nucleotide sequence ~~chosen~~ selected from the group consisting of SEQ ID No: 1, SEQ ID No: 3, SEQ ID No: 5, SEQ ID No: 7, SEQ ID No: 9, SEQ ID No: 11 and SEQ ID No: 13.

5) A DNA sequences ~~as defined in~~ of claims 1, ~~2 and 4~~ ~~characterized in that~~ wherein these DNA sequences are those of the genes coding respectively for the proteins of Candida albicans having the same functions as the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 and ~~each~~ containing a nucleotide sequence ~~chosen~~ selected from the group consisting of SEQ ID No: 1, SEQ ID No: 3, SEQ ID No: 5, SEQ ID No: 7, SEQ ID No: 9, SEQ ID No: 11 and SEQ ID No: 13.

6) A DNA sequences of genes ~~according to~~ of claim 5 ~~each~~ coding for an amino acid sequence ~~chosen~~ selected from the group consisting of SEQ ID No: 2, SEQ ID No: 4, SEQ ID No: 6, SEQ ID No: 8, SEQ ID No: 10, SEQ ID No: 12 and SEQ ID No: 14.

7) A DNA sequences coding for the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 ~~according to~~ claims 5 ~~and 6 as well as~~ and the DNA sequences which hybridizes with these and/or have significant homologies with

these sequences or the fragments ~~of these~~ thereof and code for proteins having the same functions.

8) A DNA sequence ~~according to~~ of claim 5 ~~to 7~~ comprising modifications introduced by suppression, insertion and/or substitution of at least one nucleotide coding for the proteins having the same activities as the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361.

9) A DNA sequence ~~according to one~~ of claim 5 ~~to 8 as well as~~ and ~~the~~ DNA sequences which have an homology of nucleotide sequence of at least 50 % ~~or at least 60 % and preferably at least 70 %~~ with said DNA sequences.

10) A DNA sequence ~~according to one~~ of claim 5 ~~to 9 as well as the~~ and DNA sequences which codes for the proteins with similar functions, the respective AA sequences of which have an homology of at least 40 % ~~and in particular of 45 % or of at least 50 %~~, rather at least 60 % ~~and preferably at least 70 %~~ with the AA sequences coded by said DNA sequences.

11) A Polypeptides ~~each~~ having an amino acid sequence ~~chosen~~ selected from the group consisting of SEQ ID No: 2, SEQ ID No: 4, SEQ ID No: 6, SEQ ID No: 8, SEQ ID No: 10, SEQ ID No: 12 and SEQ ID No: 14 coded by the DNA sequences ~~according to one~~ of claim 5 ~~to 10~~ and the analogues of these polypeptides.

12) A process for the preparation of recombinant proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 having respectively the amino acid sequences SEQ ID No: 2, SEQ ID No: 4, SEQ ID No: 6, SEQ ID No: 8, SEQ ID No: 10, SEQ ID No: 12 and SEQ ID No: 14 comprising, for the preparation of each of these proteins, ~~the~~ expression ~~or~~ in an appropriate host of the DNA sequence coding for this protein ~~according to one~~ of claim 5 ~~to 10, then the~~ and isolation ~~or~~ and purification ~~of~~ said recombinant protein.

13) An expression vectors ~~each~~ containing one of the DNA sequences ~~according to one~~ of claim 5 ~~to 10~~.

14) A host cell transformed with a vector ~~according to~~ claim 13.

15) A process ~~as defined in~~ of claim 12 ~~in which~~ wherein the host cell is DH5 alpha E. coli or XL1-Blue E. coli.

16) The process ~~as defined in~~ of claim 13 ~~in which~~ wherein the host cell is

Saccharomyces cerevisae.

17) ~~One or more of the~~ At least one plasmids deposited at the CNCM under the numbers I-2214, I-2215, I-2216, I-2217, I-2211, I-2212 and I-2213.

18) ~~A~~ Screening process for antifungal products ~~characterized in that it~~ comprising a stage where the activity of one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361, as defined in claim 11 is measured, in the presence of each of the products of which one wishes to determine the antifungal properties and selecting the products having an inhibitory effect on this activity ~~are selected~~.

~~19) Use of a product selected by the process according to claim 18 to obtain an antifungal agent.~~

~~20) Use of the genes of Candida albicans or of the proteins coded by these genes according to one of claims 5 to 11 for the selection of products having antifungal properties according to claim 19 as inhibitors of the proteins of Candida albicans coded by these genes.~~

21) ~~A~~ Pharmaceutical compositions containing as active ingredient at least one inhibitor of the proteins of Candida albicans ~~as defined in~~ claim 20.

~~22) Use of the compositions as defined in claim 21 as antifungal agents.~~

23) Use of a polypeptide as defined in claim 11 or a fragment of this polypeptide having the same function for the preparation of a medicament intended to induce an immunological response in a mammal by inoculation of this medicament producing an antibody which allows said mammal to be protected against the disease.

24) ~~An~~ Antibody directed against a polypeptide ~~as defined in~~ claim 11 or a fragment of this polypeptide having the same function.

25) ~~An~~ The antibody as defined in claim 24 directed against any one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 or a fragment of these proteins.

~~26) Use of any one of the genes CaDR427, CaDR789, 1CaDR527, 2CaDR527, CaFL024, CaNL260 and CaDR361 or of any one of the proteins coded by these genes according to one of claims 5 to~~

~~11 for~~ the preparation of compositions ~~which~~ can be used for the diagnosis or ~~treatment~~ of diseases caused by the ~~pathogenic~~ yeast Candida albicans.

27) A kit for the diagnosis of fungal infections comprising a DNA sequence ~~as defined in one~~ of claims 5 ~~to 10~~ or a sequence having a similar function or a functional fragment of this sequence, the polypeptide coded by this sequence or a polypeptide fragment having the same function or an antibody directed against such polypeptide coded by this DNA sequence or against a fragment of this polypeptide.

6/pats

Novel *Candida albicans* genes and proteins coded by these genes.

The present invention relates to novel *Candida albicans* genes and the proteins coded by these genes as well as the polynucleotides (RNA, DNA) coding for these proteins or for the polypeptide analogues of these proteins.

The present invention also relates to the process for the preparation of these polypeptides and polynucleotides, their use for studying pathogenic mycetes and in particular *Candida albicans* and for the preparation of inhibitors of the proteins coded by the genes of the present invention, these inhibitors being able to be used as antifungal agents. The present invention also relates to the pharmaceutical compositions containing such inhibitors.

Therefore the present invention relates in particular to novel proteins of *Candida albicans* and the nucleotide sequences coding for these proteins, their preparation and their uses.

Also hereafter the following abbreviations will be used: AA for amino acids, NA for nucleic acids, RNA for ribonucleic acid, mRNA for messenager RNA, RNase for ribonuclease, DNA for desoxyribonucleic acid, cDNA for complementary DNA, bp for base pairs, PCR for polymerase chain reaction, C.a. or *C. albicans* for *Candida albicans*, *E. coli* for *Escherichia coli* and *S. cerevisiae* for *Saccharomyces cerevisiae*.

The term screening used hereafter corresponds to the anglosaxon term screening.

The term polynucleotides designates hereafter the polynucleotides of the present invention or the DNA sequences and also RNA coding for the proteins of the present invention and their homologues coding for proteins with the same function.

The term polypeptides designates hereafter the polypeptides of the present invention or the proteins of the present invention and their functional analogues or homologues as defined hereafter, therefore having the same functions.

The term mycete designates hereafter a eucaryote organism, spore carrier, the nutrition of which occurs by absorption, which is devoid of chlorophyll and which reproduces in a sexual or asexual fashion.

Mycoses are infections of man or animals which can be superficial or deep, caused by pathogenic fungi. In the case of deep mycoses, they can be very severe and with a grave pronosis.

Antimycotic substances with fungistatic or fungicidal effects are used in the treatment of mycoses. This treatment is difficult because few available antifungal substances exist for therapeutics and they often have side effects which limit their use. For example, Amphotericin B which represents the treatment of choice for deep mycoses, has nephrotoxic side effets.

Therefore a strong demand exists for novel substances which are effective against pathogenic fungi and capable of being used in therapeutics against fungal infections. These substances could be used either in prophylaxis, in the case of severe states of immunodepression or in curative treatment of fungal infections. In addition, these substances should have a specific mode of action, allowing them to inhibit the growth or to kill the cells of mycetes without altering the essential functions of the human cells.

A subject of the present invention is to propose genes which can constitute novel targets for the identification of antifungal substances and in particular of substances allowing the treatment of the infections due to fungi of the Candida genus.

These genes are in particular essential genes which are indispensable to the survival and multiplication of the cells.

Different methods can be used for determining whether the product of a gene is essential to the survial of a mycete or essential to the establishment or maintenance of an infection. The identification of the essential character of a gene provides additional information concerning its function and allows selection of the genes the product of

which constitutes a useful target for an antifungal substance. Examples of these methods are briefly summarized hereafter. These methods are described in the following publications:

- Guthrie C. and Fink G.R. Eds. Methods in Enzymology, Vol 194, 1991, 'Guide to Yeast Genetics and Molecular Biology', Academic Press Inc.

- Pink A.H., A.E. Wheals and J.S. Harrison Eds. The yeasts, Vol.6, 1995, 'Yeast Genetics' , Academic Press Inc.

Ausubel F. et al. Eds. 'Short Protocols in Molecular Biology', 1995, Wiley.

- Brown A.J.P. and Tuite M.F. (Eds)'Yeast Gene Analysis' Methods in Microbiology, Vol 26, 1998, Academic Press Inc.

Depending on the case, one or the other of the methods described will be used as a function of the sought result. In particular, the operation can be carried out by a direct inactivation method of the gene or by a transitory inactivation method of the gene.

In the yeast *S. cerevisiae*, the most commonly used method consists in inactivating the studied gene in the yeast chromosome. The wild allele is inactivated by insertion of a genetic marker (for example an auxotrophic gene or a resistance marker). This insertion is obtained in general by the genic conversion method using linear deletion cassettes prepared according to known methods as described in Guthrie C. and Fink G.R. Eds. Methods in Enzymology, Vol 194, 1991, 'Guide to Yeast Genetics and Molecular Biology', Academic Press Inc. or in Gultner et al. Nucleic Acid Research, 1996, 24: 2519-2524.

The inactivation occurs in a diplod strain then meiosis is induced by standard methods such as for example growth in a nitrogen-poor medium and the four spores originating from individual ascus are isolated by micromanipulation. The inactivation of an essential gene translates into a loss of viability of two spores (in four) which have acquired the selection marker. The viability of these spores can be restored by the introduction into the strain of a centromeric or replicative plasmid carrying a copy of the wild gene.

The operation can also be carried out by transitory inactivation of the gene: the use of controllable promoters also allows the determination of whether a gene is essential to the survival of a cell. In order to do this, the native promoter of the gene is replaced by a promoter which is directly controllable on the chromosome or on an extra-chromosomic plasmid. For example the GAL promoter or its derivatives or the tetO promoter can be used (Mumberg et al. 1994, Nucleic Acid Research, 22: 5767-5768; Belli et al. 1998, Yeast, 14: 1127-1138). The essential character of the studied gene can thus be observed when the promoter used is repressed, either in the haploid strains in the yeast *S. cerevisiae*, or after inactivation of the second allele in diploid micro-organisms such as *C. albicans*.

Starting from an essential gene known in a species, identification can be carried out of homologous genes or genes having a similar function in another species of mycete: known methods can be used to identify the homologous genes of a studied gene in another species of mycete (so-called 'orthologous' genes) or genes with a similar function to the studied gene. Examples of methods which can be used are set out hereafter. These methods are described in the following books:

Sambrook et al. 1989, Molecular Cloning, Cold Spring Harbor Laboratory Press.

- Ausubel F. et al. Eds. 'Short Protocols in Molecular Biology', 1995, Wiley.

- Guthrie C. and Fink G.R. Eds. Methods in Enzymology, Vol 194, 1991, 'Guide to Yeast Genetics and Molecular Biology', Academic Press Inc.

The operation can be carried out for example by screening by homology, by genic complementation or also by amplification by PCR using specific probes from genomic DNA libraries or from complementary DNA (cDNA) libraries of the pathogenic mycetes.

The genomic DNA or cDNA libraries can be prepared according to known methods and the polynucleotide fragments obtained are integrated in an expression vector, for example

a vector such as pRS423 or its derivatives which are also as useful in the *E. coli* bacteria as in *S. cerevisiae*. Screening of the bank will be done by standard *in situ* hybridization methods on a replica of the bacterial colonies. The hybridization conditions are adapted to the stringency desired for the reaction, so as to identify the fragments with more or less high homology with the gene studied.

The genes of other species of mycetes can also be identified by known methods called 'genic complementation'. For example, a strain of *S. cerevisiae* in which an identified essential gene has been placed under the control of a controllable promoter can be transformed by a representative sample of a DNA or cDNA bank corresponding to the studied mycete such as *C. albicans*. When the yeasts are cultured under conditions such that the promoter is repressed, only the yeasts carrying a recombinant vector containing a functionally equivalent sequence of the studied mycete with the initial essential gene can survive. The sequence of the gene in the studied mycete is then identified by isolating the recombinant vector and by sequencing according to known methods. Similarly, the so-called 'plasmid shuffle' method allows selection of the yeasts which have lost the expression of the initial essential gene and containing a functionally equivalent sequence originating from another mycete.

The study can be carried out on different species: the functionally equivalent genes or homologues in sequence with an essential gene can be isolated in other mycetes and in particular in the different pathogenic mycetes affecting humans. For this the mycetes belonging to the Zygomycetes, Basidiomycetes, Ascomycetes and Deuteromycetes classes can in particular be used. Quite particularly, the mycetes belonging to the following sub-classes: *Candida spp.*, in particular *Candida albicans, Candida glabrata, Candida tropicalis, Candida parapsilosis and Candida krusei*. The mycetes also belonging to the following sub-classes: *Aspergillus fumigatus, Coccidioides immitis, Cryptococcus neoformans, Histoplasma capsulatum, Blastomyces dermatidis, Paracoccidioides brasiliensis and Sprorothrix schenckii*.

The present invention therefore relates to the identification of antimycotic substances such as in particular anti-*Candida albicans* substances.

The present invention therefore relates to inhibitors of fungal proteins which can be used as antifungal agents.

Thus organisms are known such as the pathogenic yeast *Candida albicans* which cause infectious diseases in the human organism. With the purpose of finding the means of treating diseases, targets can be chosen such as for example intracellular and one or more proteins of the present invention coded by the genes of the present invention can be one or some of these targets.

The present invention thus allows isolation of the DNA and RNA polynucleotides coding for the proteins of *Candida albicans* and revelation of their nucleotide sequences.

The genes of the present invention coding for the proteins of *Candida albicans* of the present invention will be called as follows: CaDR472, CaDR489, CaDR527 in the form of two different alleles namely 1CaDR527 and 2CaDR527, CaFL024, CaNL260 and CaDR361.

The nucleotide sequences of these genes (and of the two alleles for CaDR527) are given in the sequence listing hereafter and are called respectively as follows:

- SEQ ID No. 1 for CaDR472,
- SEQ ID No. 3 for CaDR489,
- SEQ ID No. 5 for the 1st allele of CaDR527 namely 1CaDR527,
- SEQ ID No. 7 for the 2nd allele of CaDR527 namely 2CaDR527,
- SEQ ID No. 9 for CaFL024,
- SEQ ID No. 11 for CaNL260
- and SEQ ID No. 13 for CaDR361.

The polypeptide sequences of the proteins coded by the genes of the present invention are called respectively as follows:

- SEQ ID No. 2 or PCaDR472 for the protein coded by CaDR472,
- SEQ ID No. 4 or PCaDR489 for the protein coded by CaDR489,
- SEQ ID No. 6 or 1PCaDR527 for the protein coded by

1CaDR527,

- SEQ ID No. 8 or 2PCaDR527 for the protein coded by 2CaDR527,
- SEQ ID No. 10 or PCaFL024 for the protein coded by CaFL024,
- SEQ ID No. 12 or PCaNL260 for the protein coded by CaNL260
- and SEQ ID No. 14 or PCaDR361 for the protein coded by CaDR361.

Therefore a subject of the present invention is isolated polynucleotides each containing a nucleotide sequence chosen from the following group:

a) a polynucleotide having at least 50 % or at least 60 % and preferably at least 70 % identity with a polynucleotide coding for a polypeptide having the same function and having an amino acid sequence homologous with a sequence chosen from SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14, as defined above and hereafter,

b) a complementary polynucleotide of polynucleotide a)

c) a polynucleotide comprising at least 15 consecutive bases of the polynucleotide defined in a) and b).

Therefore a subject of the present invention is the polynucleotides defined above such that these polynucleotides are DNA.

Therefore a subject of the present invention is the polynucleotides defined above such that these polynucleotides are RNA.

A more precise subject of the present invention is the polynucleotides as defined above each comprising a nucleotide sequence chosen from SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11 and SEQ ID No. 13 as defined above and hereafter.

The present invention thus allows the isolation of the DNA sequences coding respectively for the proteins of *Candida albicans* PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361, as defined above.

The present invention also allows revelation of the nucleic acid sequences of the genes of the present invention

and also the amino acid sequences of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361, coded by these genes.

Therefore a subject of the present invention is the DNA sequences as defined by the polynucleotides above, characterized in that these DNA sequences are those of the genes coding respectively for the proteins of *Candida albicans* (having the same functions as the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361) and each containing a nucleotide sequence chosen from SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11 and SEQ ID No. 13 as defined above and hereafter.

Such a sequence SEQ ID No. 1 of the present invention therefore comprises 747 nucleotides.

Such a sequence SEQ ID No. 3 of the present invention therefore comprises 711 nucleotides.

Such a sequence SEQ ID No. 5 of the present invention therefore comprises 1383 nucleotides.

Such a sequence SEQ ID No. 7 of the present invention therefore comprises 1383 nucleotides.

Such a sequence SEQ ID No. 9 of the present invention therefore comprises 2262 nucleotides.

Such a sequence SEQ ID No. 11 of the present invention therefore comprises 447 nucleotides.

Such a sequence SEQ ID No. 13 of the present invention therefore comprises 966 nucleotides.

A subject of the present invention is also the DNA sequences of genes as defined above each coding for an amino acid sequence chosen from SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14.

The sequence SEQ ID No. 2 of the protein PCaDR472 therefore comprises 248 AA.

The sequence SEQ ID No. 4 of the protein PCaDR489 therefore comprises 236 AA.

The sequence SEQ ID No. 6 of the protein 1PCaDR527 therefore comprises 460 AA.

The sequence SEQ ID No. 8 of the protein 2PCaDR527 therefore comprises 460 AA.

The sequence SEQ ID No. 10 of the protein PCaFL024 therefore comprises 753 AA.

The sequence SEQ ID No. 12 of the protein PCaNL260 therefore comprises 148 AA.

The sequence SEQ ID No. 14 of the protein PCaDR361 therefore comprises 321 AA.

A particular subject of the present invention is the DNA sequences coding for the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 as defined above as well as the DNA sequences which hybridize with these and/or present significant homologies with these sequences or with fragments of these and code for the proteins having the same functions.

A subject of the present invention is also the DNA sequences as defined above comprising modifications introduced by suppression, insertion and/or substitution of at least one nucleotide coding for proteins having the same activities as the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 as defined above.

In particular a subject of the present invention is the DNA sequences as defined above as well as the DNA sequences which have a nucleotide sequence homology of at least 50 % or at least 60 % and preferably at least 70 % with said DNA sequences.

Therefore a subject of the present invention is also the DNA sequences as defined above as well as the DNA sequences which code for the proteins of similar functions of which the respective AA sequences have an homology of at least 40 % and in particular of 45 % or of at least 50 %, rather at least 60 % and preferably at least 70 % with the AA sequences coded by said DNA sequences.

By sequences which hybridize are included DNA sequences which hybridize with one of the DNA sequences above under standard conditions of high, medium or low stringency and which code for polypeptides having the same function. The stringency conditions are those carried out under conditions

known to a person skilled in the art, such as those described by Sambrook et al Molecular cloning, Cold Spring Harbor Laboratory Press, 1989. Such stringency conditions are for example hybridization at 65°C, for 18 hours in a 5 x SSPE; 10 x Denhardt's; 100μg/ml ssDNA; 1 % SDS solution followed by washing 3 times for 5 minutes with 2 x SSC; 0.05 % SDS, then washing 3 times for 15 minutes at 65°C in 1 x SSC; 0.1 % SDS. The high stringency conditions for example include hybridization for 18 hours at 65°C in a 5 x SSPE; 10 x Denhardt's; 100μg/ml ssDNA; 1 % SDS solution, followed by washing twice for 20 minutes with a 2 x SSC; 0.05 % SDS solution at 65°C followed by a final wash for 45 minutes in a 0.1 x SSC; 0.1 % SDS solution at 65°C. Medium stringency conditions for example include a final washing for 20 minutes in a 0.2 x SSC, 0.1 % SDS solution at 65°C.

By sequences which have significant homologies are included the sequences having a moderate or considerable identity of nucleotide sequence with one of the DNA sequences above and which code for a protein having the same function.

By sequence of similar DNA, is thus meant the DNA sequences which can belong to mycetes other than *Candida albicans* and in particular to S.c. and which are similar or identical to the DNA sequences of the genes of *Candida albicans* as defined above. These similar DNA sequences are not necessarily identical to the DNA sequences of the genes as defined above. The homology of sequence at the nucleotide level can be moderate or considerable. The present invention thus relates in particular to the DNA sequences which have an homology of nucleotide sequence of at least 50 %, of preferably at least 60 % and even more preferably of at least 70 % with the sequences of the genes of the present invention.

Moreover, these similar DNA sequences do not necessarily code for identical proteins, at the level of the amino acid sequences to the proteins coded by the genes as defined above. Thus the present invention relates in particular to the DNA sequences which code for the so-called homologous proteins having an homology of amino acid sequence of at

least 40 %, in particular 45 %, preferably at least of 50 %, more preferably at least of 60 % and yet more preferably at least of 70 % with the proteins coded by the genes of the present invention.

Each gene of the present invention is represented as a single strand DNA sequence as indicated in SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11 and SEQ ID No. 13 represented respectively in the sequence listing hereafter, but it is understood that the present invention includes the complementary DNA sequence of this single strand DNA sequence and also includes the so-called double strand DNA sequence constituted by these two DNA sequences complementary to one another.

The DNA sequences as defined above are examples of the combination of codons coding for the amino acids corresponding respectively to the amino acid sequences SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14, as defined above, but it is also understood that the present invention includes any other arbitrary combination of codons coding for these same amino acid sequences.

For the preparation of the polynucleotides and in particular of the DNA sequences as defined above, the DNA sequences modified as indicated above or also the homologous DNA sequences as defined above, the techniques known to a person skilled in the art can be used and in particular those described in the work by Sambrook, J. Fritsh, E. F. § Maniatis, T. (1989) entitled: 'Molecular cloning: a laboratory manual , Laboratory, Cold Spring Harbor NY.

The homologous DNA sequences as defined above can in particular be isolated according to the methods known to a person skilled in the art for example by the PCR technique using degenerated nucleotide primers to amplify this DNA from genome or cDNA libraries of the corresponding mycetes. The cDNA can also be prepared from mRNA isolated from mycetes of different species studied within the scope of the present invention such as *Candida albicans* but for example and quite as well: *Candida stellatoidea, Candida tropicalis, Candida*

parapsilosis, Candida krusei, Candida pseudotropicalis, Candida quillermondii, Candida glabrata, Candida lusianiae or Candida rugosa or also mycetes such as *Saccharomyces cerevisiae or also the mycetes of Aspergillus or Cryptococcus type and in particular, for example, Aspergillus fumigatus, Coccidioides immitis, Cryptococcus neoformans, Histoplasma capsulatum, Blastomyces dermatitidis, Paracoccidioides brasiliens and Sporothrix schenckii* or also the mycetes of the phycomycetes or eumycetes classes in particular the sub-classes of basidiomycetes, ascomycetes, mehiascomycetales (yeast) and plectascales, gymnascales (fungi of the skin and hair) or of the hyphomycetes class, in particular the sub-classes conidiosporales and thallosporales amongst which the following species: mucor, rhizopus, coccidioides, paracoccidioides (blastomyces, brasiliensis), endomyces (blastomyces), aspergillus, menicilium (scopulariopsis), trichophyton (ctenomyces), epidermophton, microsporon, piedraia, hormodendron, phialophora, sporotrichon, cryptococcus, candida, geotrichum, trichosporon or also toropsulosis.

The polynucleotides of the present invention can thus be obtained by using the usual cloning and screening methods such as those of cloning and sequencing from fragments of chromosomal DNA extracted from cells or also originating from gene banks. For example, in order to obtain the polynucleotides of the present invention, a bank of chromosomal DNA fragments can be used. A probe corresponding to an oligonucleotide labelled with a radioactive element, preferably constituted by 17 or also 20 or more nucleotides and derived from a partial sequence can be prepared. The clones containing DNA identical to that of the probe can be identified in this way under stringent conditions. By the sequencing of the individual clones identified in this way, using the sequencing primers originating from the original sequence, it is then possible to extend the sequence in both directions in order to determine the complete gene sequence. In a usual and efficient fashion, such sequencing can be carried out by using denatured double strand DNA prepared

from a plasmid. Such techniques are described by Maniatis, T. Fritsch, E.F. and Sambrook as indicated above.(Laboratory Manual, Cold Spring Harbor, New York (1989) (in particular in 1.90 and 13.70 in the chapters on screening by hybridization and sequencing from denatured double strand DNA).

Within the scope of the present invention, a bank of chromosomal DNA fragments of *Candida albicans* can in particular be used as indicated hereafter in the examples described in the experimental part.

A detailed description of the operating conditions in which the present invention has been carried out is given below.

A quite particular subject of the invention is the polypeptides each having an amino acid sequence chosen from SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14, coded by the DNA sequences as defined above and the analogues of these polypeptides.

By polypeptide analogues, are understood polypeptides, the amino acid sequence of which has been modified by substitution, suppression or addition of one or more amino acids but which retain the same biological function. Such polypeptide analogues can be produced spontaneously or can be produced by post-transcriptional modification or also by modification of the DNA sequence of the present invention as indicated above, using techniques known to a person skilled in the art: amongst these techniques, the technique of directed mutagenesis known to a person skilled in the art (Kramer, W., et al., Nucl. Acids Res., 12, 9441 (1984); Kramer, W. and Fritz, H.J., Methods in Enzymology, 154, 350 (1987); Zoller, M.J. and Smith, M. Methods in Enzymology, 100, 468 (1983)) can in particular be mentioned.

Modified DNA synthesis can be carried out as indicated above and in particular by using well known chemical synthesis techniques such as for example the phosphotriester method [Letsinger, R.L and Ogilvie, K.K., K. Am. CHEM. Soc., 91, 3350 (1969); Merrifield, R.B., Sciences, 150, 178 (1968)] or the phosphoamidite method [Beaucage, S.L and

Caruthers, M .H., Tetrahedron Lett., 22, 1859 (1981); McBRIDE, L.J. and Caruthers, M.H. Tetrahedron Lett., 24 245 (1983)] or also the combination of these methods.

The polypeptides of the present invention can therefore be prepared using techniques known to a person skilled in the art, in particular partially by chemical synthesis or also by the recombinant DNA technique by expression in a procaryotic or eucaryotic host cell as indicated hereafter.

A particular subject of the present invention is the process for the preparation of recombinant proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 having respectively the amino acid sequences SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14, as defined above, comprising, for the preparation of each of these proteins, the expression in an appropriate host of the DNA sequence as defined above coding for this protein then the isolation and the purification of said recombinant protein.

To produce the polypeptides of the present invention, recombinant DNA techniques using genetic engineering and cell culture methods known to a person skilled in the art can in particular be used. The following stages can then be carried out: firstly preparation of the appropriate gene, then incorporation of this gene into a vector, transfer of the carrier vector of the gene into an appropriate host cell, production of the polypeptide by expression of the gene, isolation of the polypeptide, the polypeptide thus produced can then be purified.

The polypeptides of the present invention obtained by expression of the polynucleotides of the present invention can be purified from cell cultures transformed by methods well known to a person skilled in the art such as precipitation with ammonium sulphate or ethanol, extraction under acid conditions, anion or cation exchange chromatography, hydrophobic interaction chromatography, affinity chromatography, hydroxylapatite chromatography and high performance liquid chromatography (HPLC). Techniques well known to a person skilled in the art can be used to

regenerate the protein when it is denatured during its isolation or purification.

The DNA sequences according to the present invention and in particular SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11 and SEQ ID No. 13 can be prepared according to techniques known to a person skilled in the art in particular by chemical synthesis or by screening of a gene bank or a cDNA bank using synthetic oligonucleotide probes by known hybridization techniques, as well as amplification of DNA from isolated fragments or also by reverse transcriptase from messenger RNA (mRNA).

The advantage of the technique comprising firstly the isolation of mRNA by extraction of the total RNA then the synthesis of cDNA from these mRNA by reverse transcriptase in particular rests on the fact that the mRNA does not contain introns even though these non-coding sequences can be present in the genomic DNA.

The usual cloning techniques known to a person skilled in the art and in particular described in the book by Sambrook, J. Fritsh, E. F. § Maniatis, T. (1989) entitled: 'Molecular cloning: a laboratory manual, Laboratory, Cold Spring Harbor NY can then be carried out.

In these techniques, cloning can be carried out by insertion of a fragment into a plasmid which can be provided with a suitable commercial kit then transformation of a bacterial strain by the plasmid thus obtained. In particular the XL1 Blue or DH5 alpha *E. coli* strain can be used. The clones can then be cultured in order to extract the plasmid DNA according to standard techniques known to a person skilled in the art referred to above (Sambrook, Fritsh and Maniatis). The DNA sequencing of the amplified fragment contained in the plasmid DNA can then be carried out.

The polypeptides of the present invention can be obtained by expression in a host cell containing a polynucleotide according to the present invention and in particular a DNA sequence coding for a polypeptide of the present invention preceded by a suitable promoter sequence. The host cell can be a procaryotic cell, for example *E. coli*

or a eucaryotic cell such as yeasts such as for example Ascomycetes amongst which is Saccharomyces or also mammalian cells such as Cos cells for example.

A particular subject of the present invention is the expression vectors each containing one of the DNA sequences of the present invention as defined above.

In each of these expression vectors, such a DNA sequence is therefore in particular the DNA sequence of a gene of the present invention coding for a protein of *Candida albicans* and containing a nucleotide sequence chosen from SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11 and SEQ ID No. 13.

In each of these expression vectors, such a DNA sequence is thus even more particularly that of the genes as defined above coding for one of the amino acid sequences SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14 as defined above and hereafter.

In each of the expression vectors of the present invention, such a DNA sequence is thus a DNA sequence as defined above coding for one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 as well as the DNA sequences which hybridize with this and/or have significant homologies with this sequence or with the fragments of this or also the DNA sequences comprising modifications introduced by suppression, insertion and/or substitution of at least one nucleotide coding for a protein having the same activity.

In each of the expression vectors, such a DNA sequence is in particular a DNA sequence as defined above as well as similar DNA sequences which have a nucleotide sequence homology of at least 50 % or at least 60 % and preferably at least 70 % with said DNA sequence or also similar DNA sequences which code for a protein, the AA sequence of which has an homology of at least 40 % and in particular of 45 % or of at least 50 %, rather at least 60 % and preferably at least 70 % with the AA sequence coded by said DNA sequence.

The expression vectors are vectors allowing the

expression of the protein under the control of a suitable promoter. Such a vector can be a plasmid, a cosmid or viral DNA. For the procaryotic cells, the promoter can for example be the lac promoter, the trp promoter, the tac promoter, the β-lactamase promoter or the PL promoter. For the yeast cells, the promoter can be for example the PGK promoter or the GAL promoter. For mammalian cells, the promoter can for example be the SV40 promoter or adenovirus promoters.

Baculovirus type vectors can also be used for the expression in insect cells.

The host cells are for example procaryotic cells or eucaryotic cells. The procaryotic cells are for example *E. coli*, Bacillus or Streptomyces. The eucaryotic host cells include yeasts as well as cells of higher organisms, for example mammalian cells or insect cells. The mammalian cells are for example hamster CHO or BHK cells and monkey Cos cells. The insect cells are for example SF9 cells.

The present invention therefore relates to a process which comprises the expression of a polynucleotide according to the present invention coding for one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 in a host cell transformed by a polynucleotide according to the present invention and in particular a DNA sequence coding for the amino acid sequence SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14. In the implementation of such a process, the host cell is in particular a eucaryote cell.

For the implementation of the present invention, the vectors used can for example be pGEX or pBAD and the host cell can be *E. coli* or for example the vector pYX222 and the host cell can be in particular *Saccharomyces cerevisiae*.

A particular subject of the present invention is the host cell transformed with a vector as defined above and containing a DNA sequence according to the present invention.

A subject of the present invention is therefore the process for the preparation of a recombinant protein according to the present invention, as defined above, in which the host cell is DH5 alpha *E. coli* or XL1-Blue *E. coli*

or in particular *Saccharomyces cerevisiae*.

A detailed account of the conditions under which the operations indicated above can be carried out is given hereafter in the experimental part. A plasmid is thus obtained in which the gene of the present invention is inserted and this plasmid introduced into a host cell is then obtained by operating according to the usual techniques known to a person skilled in the art.

A very precise subject of the present invention is the 7 plasmids deposited on the 25th May 1999 at the Collection Nationale de Cultures de Microorganismes (CNCM) - INSTITUT PASTEUR - 25, rue du Docteur Roux - 75724 PARIS Cedex 15 under the following numbers: I-2214, I-2215, I-2216, I-2217, I-2211, I-2212 and I-2213.

I-2214 is the registration number of the strain CaDR472.10 constituted by the bacteria XL1-blue *E. coli* containing a plasmid carrying the gene of *Candida albicans* CaDR472 of the present invention prepared as indicated in Example 1 of the present invention.

This gene therefore corresponds to the sequence CaDR472 of SEQ ID No. 1.

I-2215 is the registration number of the strain CaDR489.37 constituted by the bacteria XL1-blue *E. coli* containing a plasmid carrying the gene of *Candida albicans* CaDR489 of the present invention prepared as indicated in Example 2 of the present invention.

This gene therefore corresponds to the sequence CaDR489 of SEQ ID No. 3.

I-2216 is the registration number of the strain CaDR527.2 constituted by the bacteria XL1-blue *E. coli* containing a plasmid carrying the gene of *Candida albicans* CaDR527 (allele 1) of the present invention prepared as indicated in Example 3 of the present invention.

This gene therefore corresponds to the sequence 1CaDR527 of SEQ ID No. 5.

I-2217 is the registration number of the strain CaDR527.3 constituted by the bacteria XL1-blue *E. coli* containing a plasmid carrying the gene of *Candida albicans*

CaDR527 (allele 2) of the present invention prepared as indicated in Example 3 of the present invention.

This gene therefore corresponds to the sequence 2CaDR527 of SEQ ID No. 7.

I-2211 is the registration number of the strain CaFL024.4 constituted by the bacteria XL1-blue *E. coli* containing a plasmid carrying the gene of *Candida albicans* CaFL024 of the present invention prepared as indicated in Example 4 of the present invention.

This gene therefore corresponds to the sequence CaFL024 of SEQ ID No. 9.

I-2212 is the registration number of the strain CaNL260.4 constituted by the bacteria XL1-blue *E. coli* containing a plasmid carrying the gene of *Candida albicans* CaNL260 of the present invention prepared as indicated in Example 5 of the present invention.

This gene therefore corresponds to the sequence CaNL260 of SEQ ID No. 11.

I-2213 is the registration number of the strain CaDR361.3 constituted by the bacteria XL1-blue *E. coli* containing a plasmid carrying the gene of *Candida albicans* CaDR361 of the present invention prepared as indicated in Example 6 of the present invention.

This gene therefore corresponds to the sequence CaDR361 of SEQ ID No. 13.

Therefore a very precise subject of the present invention is one or more of the plasmids deposited under the numbers I-2214, I-2215, I-2216, I-2217, I-2211, I-2212 and I-2213.

The operating conditions under which the present invention was carried out are described hereafter in the experimental part.

Therefore a subject of the present invention is a screening process for antifungal products characterized in that it comprises a stage where the activity of one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 as defined above is measured in the presence of each of the products the antifungal properties of

which one wishes to determine and the products having an inhibitory effect on this activity are selected.

In particular, the genes coding for the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 of the present invention being essential to the survival of the cells of *Candida albicans*, of the inhibitory substances of such proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 could be of use as antifungal agents, either as medicaments or on the industrial level.

For example, to screen antifungal substances such as the substances active on *Candida albicans,* the activity of a protein coded by a gene of the present invention or one of its functional homologues is measured and the protein is put in the presence of each of the products the antifungal properties of which one wishes to determine and the products having an inhibitory effect on this activity are selected.

Such screening can be carried out by measuring the activity of one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 of the present invention in the presence of potential activators or inhibitors to be tested, for example by measuring in vitro in an appropriate reaction medium.

The activity of the proteins of the present invention can also be measured *in vivo* by an appropriate cell test. For example, the activity of PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 can be advantageously measured in cells of a mutant of *Saccharomyces cerevisiae* transformed by one of the genes of the present invention and not expressing the homologous protein PYDR 472w, PYDR 489w, PYDR 577w, PYFL 024c, PYNL 260c and PYDR 361c of *Saccharomyces cerevisiae*.

The invention also encompasses the use of a product selected as indicated above for its inhibitory properties on one of the proteins of the present invention for obtaining of an antifungal agent.

The present invention is better understood using the experimental part which follows and which describes the

cloning of genes CaDR472, CaDR489, 1CaDR527, 2CaDR527, CaFL024, CaNL260 and CaDR361 of the present invention.

Therefore a subject of present invention is the use of a product selected by the process of screening antifungal products as defined above for obtaining an antifungal agent.

A subject of the present invention is also the use of the genes of *Candida albicans* of the present invention or of the proteins coded by these genes as defined above for the selection of products having antifungal properties as defined above and used as inhibitors of the proteins of *Candida albicans* coded by these genes.

A subject of present invention is also the pharmaceutical compositions containing as active ingredient at least one inhibitor of the proteins of *Candida albicans* of the present invention as defined above.

Such compositions can in particular be useful for treating topical and systemic fungal infections.

The pharmaceutical compositions indicated above can be administered by buccal, rectal, parenteral route or by local route as a topical application on the skin and mucous membranes or by injection by intravenous or intramuscular route. These compositions can be solid or liquid and be presented in all the pharmaceutical forms commonly used in human medicine such as, for example, plain or sugar coated tablets, gelatin capsules, granules, suppositories, injectable preparations, ointments, creams, gels and aerosol preparations; they are prepared according to the usual methods. The active ingredient can be incorporated in excipients normally used in these pharmaceutical compositions, such as talc, gum arabic, lactose, starch, magnesium stearate, cocoa butter, aqueous or non aqueous vehicles, fatty substances of animal or vegetable origin, paraffin derivatives, glycols, various wetting, dispersing or emulsifying agents, and preservatives.

The dose will be variable according to the product used, the subject treated and the disease in question.

A particular subject of the present invention is thus the use of compositions as defined above as antifungal

agents.

A subject of the present invention is also a method of inducing an immunological response in a mammal comprising the inoculation of this mammal with a polypeptide according to the present invention as defined above or a fragment of this polypeptide having the same function in order to produce an antibody protecting the mammal against the disease.

Therefore a subject of the present invention is also the use of a polypeptide as defined above or a fragment of this polypeptide having the same function for the preparation of a medicament intended to induce an immunological response in a mammal by inoculation with this medicament producing an antibody protecting the animal against the disease.

A subject of the present invention is also the antibodies directed against the polypeptides of the present invention as defined above or against a fragment of these polypeptides having the same function and coded by the polynucleotides of the present invention and in particular by a DNA sequence as defined above.

The polypeptides of the present invention can thus be used as immunogens to produce immunospecific antibodies of these polypeptides. The term antibody used designates antibodies which can equally be monoclonal, polyclonal, chimeric, single chain, non-human antibodies and human antibodies, as well as Fab fragments, including the products of a Fab immunoglobulin bank. The antibodies produced against the polypeptides of the present invention can be obtained by administration of the polypeptides of the present invention or fragments carrying epitopes, their analogues or also animal cells, preferably non-human, by using routine protocols for the preparation of monoclonal antibodies. Such antibodies can be prepared by methods well known in this field such as those described in the book Antibodies, Laboratory manual Ed. Harbow and David Larre, Cold Spring Harbor laboratory Eds, 1988.

Therefore a quite particular subject of the present invention is an antibody directed against any one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024,

PCaNL260, PCaDR361 of the present invention or a fragment of these proteins. Such a fragment has in particular the same function as the protein from which it originated.

A subject of the present invention is also the use of genes CaDR472, CaDR489, 1CaDR527, 2CaDR527, CaFL024, CaNL260 and CaDR361 of the present invention or of the proteins coded by these genes as defined above for the preparation of compositions which can be used for the diagnosis or treatment of diseases caused by the pathogenic yeast *Candida albicans*.

The present invention also relates to the use of the polynucleotides of the present invention as diagnostic reagents. The detection of a polynucleotide according to the present invention coding for one of the proteins of *Candida albicans* of the present invention or of its analogues in a eucaryote in particular a mammal and more particularly a human being, can constitute a means of diagnosing a disease: thus, such a polynucleotide according to the present invention and in particular a DNA sequence can be detected by a wide variety of techniques in a eucaryote in particular a mammal and more particularly a human being, infected by an organism containing at least one of the polynucleotides of the present invention. The nucleic acids for such a use as a diagnostic tool can be detected in infected cells or tissues, such as bone, blood, muscle, cartilage or skin. For this detection, the genomic DNA can be used directly or also be amplified by PCR or another amplification technique. The RNA or DNA and cDNA can also be used with the same purpose. By amplification techniques, the line of the mycete present in a eucaryote in particular a mammal and more particularly a human being, can be characterized by analysis of the genotype. Deletions or insertions can be detected by a change in the size of the amplified product in comparison with the genotype of the reference sequence. The points of mutation can be identified by hybridization of the DNA amplified with the sequences, labelled by a radioactive element, of polynucleotides of the present invention. Perfectly complementary sequences can therefore be distinguished from duplexes which poorly resist digestion by nucleases. The DNA

sequence differences can also be detected by alterations in the electrophoretic mobility of DNA fragments in gels, with or without denaturing agent, or by direct DNA sequencing (reference: Myers et al. Science, 230: 1242 (1985)).

Sequence changes at specific locations can also be revealed by protection experiments against nucleases such as RNase I and S1 or by chemical cleavage methods (reference: Cotton et al., Proc Natl Acad Sci, USA, 85: 4397-4401 (1985).

Cells containing one of the polynucleotides of the present invention carrying mutations or polymorphisms can also be detected by a large number of techniques making it possible in particular to determine the serotype. For example, the RT-PCR technique can be used to detect the mutations. It is particularly preferable to use RT-PCR techniques in conjunction with automatic detection systems, such as for example the GeneScan technique. RNA and cDNA can be used in the PCR or RT-PCR techniques. For example, complementary primers of polynucleotides coding for the polypeptides of the present invention can be used to identify and analyse the mutations.

Primers can therefore be used to amplify an isolated DNA from the infected individual. In this way mutations in the DNA sequence can be detected and used to diagnose the infection and determine the serotype or the classification of the infectious agent. Such techniques are standard for a person skilled in the art and are described in particular in the manual 'Current Protocols in Molecular Biology', Ausubel et al, ed. John Wiley § sons, Inc., 1995).

The present invention therefore relates to a process of diagnosing a disease and preferably a fungal infection caused by *Candida albicans* such as mycoses as indicated above, this process comprising the determination from a sample taken from an infected individual, an increase in the quantity of one of the polynucleotides of the present invention. Such a polynucleotide can in particular have a DNA sequence of the present invention as defined above.

Increases or reductions in the quantity of polynucleotides can be measured by techniques well known to a person skilled

in the art such as in particular amplification, PCR, RT PCR, Northern blotting or other hybridization techniques.

In addition, a diagnosis method in accordance with the present invention consists of the detection of too large an expression of polypeptides of the present invention, in comparison with control samples constituted by normal, non-infected tissues used to detect the presence of an infection.

The techniques which can therefore be used to detect the quantities of proteins expressed in a host cell sample are well known to a person skilled in the art. For example radioimmunoassay or competitive-binding techniques, Western Blot analysis and ELISA test (ref Ausubel indicated above) can thus be mentioned.

A subject of the present invention is also a kit for the diagnosis of fungal infections comprising a DNA sequence according to the present invention as defined above or a similar sequence or a functional fragment of this sequence, the polypeptide coded by this sequence or a polypeptide fragment having the same function or an antibody directed against such a polypeptide coded by this DNA sequence or against a fragment of this polypeptide.

This kit can thus contain a DNA sequence according to the present invention as defined above either for example the DNA sequence SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11 or SEQ ID No. 13 or a fragment of this sequence.

Such a kit can similarly contain a polypeptide according to the present invention or a fragment of this polypeptide and in particular one of the proteins according to the present invention having the AA sequence SEQ ID No: 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14 or also an antibody as defined above.

Such a kit can be prepared according to methods well known to a person skilled in the art.

The sequence listing SEQ ID No. 1 to SEQ ID No. 32 and Figures 1 to 6 hereafter show the following illustrations which allow a better description of the present invention..

Sequences SEQ ID No. 1 to SEQ ID No. 32 represent the

nucleotide or peptide sequences indicated in the present invention.

Sequences SEQ ID No. 1 to SEQ ID No. 14 describe the nucleotide sequences of the genes of *Candida albicans* of the present invention and the peptide sequences of the proteins derived from these genes.

Sequences SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11 or SEQ ID No. 13 thus respectively describe the nucleotide sequences of the genes of *Candida albicans* of the present invention: CaDR472, CaDR489, 1CaDR527, 2CaDR527, CaFL024, CaNL260 and CaDR361.

Sequences SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14 respectively describe the peptide sequences of the proteins derived from the genes of the present invention.

Thus, for example, sequences SEQ ID No. 1 and SEQ ID No. 2 respectively represent the nucleotide sequence of the gene CaDR472 and the peptide sequence of the protein derived from this gene namely PCaDR472.

Sequences SEQ ID No. 15 to SEQ ID No. 20 respectively represent the sequences of the 6 probes used for the preparation of the genes of *Candida albicans* of the present invention as indicated hereafter in the experimental part.

Sequences SEQ ID No. 21 to SEQ ID No. 32 respectively represent the sequences of the 2 x 6 oligonucleotides used to amplify the probes for the preparation of the genes of *Candida albicans* of the present invention as indicated hereafter in the experimental part.

Figures 1 to 6 hereafter each refer respectively to one of the 6 preparations of the genes of *Candida albicans* of the present invention namely: CaDR472, CaDR489, 1CaDR527/2CaDR527, CaFL024, CaNL260 and CaDR361, these preparations being described hereafter in the experimental part in Examples 1 to 6.

Each of Figures 1 to 6 describe the comparison of the protein derived from the probe used for the preparation of one of the genes of *Candida albicans* of the present invention (the 6 probes used having sequences SEQ ID No. 15 to SEQ ID

No. 20) with the sequence of the gene of S.c. taken as a starting point of the preparation of this gene of *Candida albicans*.

Thus, with reference to Example 1 of the preparation of the gene CaDR472 of the present invention, Figure 33 represents the comparison of the protein derived from the probe of CaDR472 (SEQ ID No. 15) with the protein derived from the gene YDR472w of *S. cerevisiae*.

The experimental part hereafter allows the description the present invention without however limiting it.

Experimental part

EXAMPLE 1: Cloning and sequencing of the gene CaDR472 (method A)

The Stanford Internet site (http://candida.standford.edu/) allows direct access to the preliminary sequences of the genome of *Candida albicans*. One of these sequences has an homology with the gene YDR472w of *S. cerevisiae*. Two oligonucleotides have been chosen in this sequence namely:

5'CAATTTATTC ATGTTCGNAT CTGGAAATTG ATTTT3' called SEQ ID No. 21 and 5'CCAAATCTCA AACTCTCTCT AATTAAAAC3' called SEQ ID No. 22.

These two oligonucleotides are used to amplify the fragment of *C. albicans*. After cloning, a so-called probe sequence of CaDR472 of 320 base pairs close to the expected sequence was obtained: the probe of CaDR472 is called SEQ ID NO 15. The protein derived from the probe of CaDR472 (SEQ ID NO 15) was compared to that of YDR472w which demonstrates an identity of 48% between these two AA sequences: this comparison is represented in Figure 1.

The fragment of 320 base pairs of *C. albicans* was used as a probe for screening the gene bank of *C. albicans*: this bank of C.a. was prepared by partial digestion of the genomic DNA of *C. albicans* by Sau3AI and cloning in the vector YEP24 at the BamHI restriction site. The clones of the gene bank were then plated at the density of 2000 clones per dish: each dish is then covered with a nitrocellulose filter which is successively treated with: NaOH, 0.5M, for 5 minutes; Tris,

1M, pH 7.7, for 5 minutes; Tris , 0.5M, pH 7.7, NaCl , 1.25M, for 5 minutes. After drying, the filters are kept for two hours at 80°C. Prehybridization and hybridization are carried out in a buffer of 40 % formamide, 5xSSC, 20 mM Tris pH 7.7 1xDenhardt 0.1 % SDS. The probe is then labelled with P32 using the Rediprime and dCTP 32p kit from Amersham UK. Hybridization is carried out for 17 hours at 42°C. The filters are then washed with 1xSSC, 0.1 % SDS, three times for 5 minutes at ambient temperature and then twice for 30 minutes at 60°C then subjected to an autoradiography overnight. The colonies corresponding to the spots obtained are isolated by a new plating at low density followed by hybridization: 8 positive clones are thus obtained (from 60 000) which are then sequenced using an ABI 377 device. Sequences are compiled using ABI software then analyzed using a GCG software package. One of the 8 clones is shown to contain the complete coding sequence corresponding to the probe used: this gene is called CaDR472 and this sequence is called SEQ ID NO 1.

CaDR472 has 47.5 % of nucleotides identical to YDR472w of *S. cerevisiae*.

For the translation to amino acids, account was taken of the fact that in *C. albicans* the CTG codon is translated to serine (there is one CTG codon in CaDR472). The protein derived from the gene CaDR472 (SEQ ID No. 1) namely SEQ ID No. 2 (PCaDR472) has 52.4 % similarity in amino acids and 44 % identity in amino acids with the protein derived from YDR472w.

The complete sequence of the gene CaDR472 contains a CTG codon.

EXAMPLE 2: Cloning and sequencing of the gene CaDR489

The operation is carried out as in Example 1 starting from preliminary sequences of the genome of *Candida albicans* from the Stanford Internet site (http://candida.standford.edu/). One of these sequences has an homology with the gene YDR489w of *S. cerevisiae*. Two oligonucleotides were chosen in this sequence namely: 5'GTTCATGTTT GGTGACTCAG AGCGTCTCAA CTATATTG3' called SEQ ID

No. 23
and 5'TTTGATAAAC ACAGGCTGGT CTAAATCTGG CTC3' called SEQ ID No. 24.

These two oligonucleotides are used to amplify the fragment of *C. albicans*. After cloning, a so-called probe sequence of CaDR489 of 295 base pairs close to the expected sequence was obtained: the probe of CaDR489 is called SEQ ID No. 16. The protein derived from the probe of CaDR489 (SEQ ID No. 16) was compared to that of YDR489w which demonstrates an identity of 41% between these two AA sequences: this comparison is represented in Figure 2.

The fragment of 295 base pairs of *C. albicans* was used as probe for screening the gene bank of *C. albicans* prepared by partial digestion of the genomic DNA of *C. albicans* proceeding as in Example 1.

The cloning is carried out as indicated in Example 1 and after prehybridization and hybridization carried out as indicated in Example 1, 4 positive clones are obtained (from 40 000). The sequencing and analyzing of the sequences obtained as indicated in Example 1, and thus a clone is obtained shown to contain the complete coding sequence corresponding to the probe used: this gene is called CaDR489 and this sequence is called SEQ ID No. 4.
CaDR489 has 48.1 % of nucleotides identical to YDR489w of *S. cerevisiae*.

The protein derived from the gene CaDR489 (SEQ ID No. 3) namely SEQ ID No. 4 or PcaDR489 has 50 % similarity in amino acids and 37 % of identity in amino acids with the protein derived from YDR489.

The complete sequence of the gene CaDR489 contains a CTG codon.

EXAMPLE 3: Cloning and sequencing of the gene CaDR527

The operation is carried out as in Example 1 starting from preliminary sequences of the genome of *Candida albicans* from the Stanford Internet site (http://candida.standford.edu/). One of these sequences has an homology with the gene YDR527w of *S. cerevisiae*. Two oligonucleotides have been chosen in this sequence namely:

5'ATCTCTGATA TGAGATTTGG CTTTAAAGGC GA3' called SEQ ID No. 25 and 5'GGTCTTTTTT CCATCAGCTG CCTCTGTTAT TG3' called SEQ ID No. 26.

These two oligonucleotides are used to amplify the fragment of *C. albicans*. After cloning, a so-called probe sequence of CaDR527 of 392 base pairs close to the expected sequence was obtained: the probe of CaDR527 is called SEQ ID No. 17. The protein derived from the probe of CaDR527 (SEQ ID No. 17) was compared to that of YDR527w which demonstrates an identity of 41% between these two AA sequences: this comparison is represented in Figure 3.

The fragment of 392 base pairs of *C. albicans* was used as probe for the screening of the gene bank of *C. albicans* prepared by partial digestion of the genomic DNA of *C. albicans* proceeding as in Example 1.

The cloning is carried out as indicated in Example 1 and after prehybridization and hybridization carried out as indicated in Example 1, 7 positive clones are obtained (from 40 000). The sequencing and analysis of the sequences obtained is carried out as indicated in Example 1.

Thus two clones obtained are each shown to contain a complete coding sequence each corresponding to an allele of the probe used: this gene is called CaDR527 and the two alleles are thus called 1CaDR527 and 2CaDR527 and their respective sequences are respectively called SEQ ID No. 5 and SEQ ID No. 7.

It is noted that the genes of the alleles 1CaDR527 and 2CaDR527 (SEQ ID No. 5 and SEQ ID No. 7) differ by 13 nucleotides.

The gene CaDR527 (1st allele) has 53.8 % of nucleotides identical to YDR527w of *S. cerevisiae*.

The proteins derived from these alleles namely SEQ ID No. 6 (PCaDR527) for the 1st allele 1CaDR527 and SEQ ID No. 8 for the 2nd allele 2CaDR527 differ between themselves by 5 amino acids.

The protein derived from the gene CaDR527 (SEQ ID No. 6) has 58.9 % similarity in amino acids and 47.9 % identity in amino acids with the protein derived from YDR527.

The complete sequence of the gene CaDR527 does not contain a CTG codon.

EXAMPLE 4: Cloning and sequencing of the gene CaFL024 (method B)

The Stanford Internet site (http://candida.standford.edu/) allows direct access to the preliminary sequences of the genome of *Candida albicans*. One of these sequences has an homology with the gene YFL024c of *S. cerevisiae*. Two oligonucleotides were chosen in this sequence namely:
5' ATTCCCACAC CGGACGCTTC 3' called SEQ ID No. 27
and 5'GACAACTCCT CGTACGATAG 3' called SEQ ID No. 28.

These two oligonucleotides are used to amplify the fragment of *C. albicans*. After cloning, a so-called probe sequence of CaFL024 of 335 base pairs close to the expected sequence was obtained: the probe of CaFL024 is called SEQ ID No. 18. The protein derived from the probe of CaFL024 (SEQ ID No. 18) was compared to that of YFL024c which demonstrates a similarity of 62 % and an identity of 58 % between these two AA sequences: this comparison is represented in Figure 4.

This fragment of 335 base pairs of *C. albicans* was used as probe for screening a gene bank of *C. albicans*: this bank of genes of C.a. was prepared by partial digestion of the genomic DNA of *C. albicans* by SauIIIA and cloning in the vector YEP-24 at the BamHI restriction site. The clones of the gene bank were then plated at a density of 2000 clones per dish: each dish is then covered with a nitrocellulose filter which is successively treated with: 1.5 M NaCl/ 0.5 M NaOH for 5 minutes; 1.5 M NaCl/0.5 M Tris-HCl pH 7.2/1 mM EDTA for 3 minutes, twice.

The DNA is then 'crosslinked' to the filter (Amersham Life Science, ultraviolet crosslinker).

The probe (100 ng) is then labelled with P32 using the Rediprime and dCTP kit (Amersham Life Science).

Prehybridization and hybridization of the filters are carried out in a buffer of 30 % of formamide, 5 x SSC, 5 % of Denhardt's solution, 1 % SDS, 100 µg/ml of salmon sperm DNA and a concentration of the probe of 10(6) cpm/ml: the hybridization is carried out at 42°C for 16 hours.

The filters are then washed three times, for 5 minutes each time, at ambient temperature with 2 x SSC/ 0.1 % SDS then three times with 1 x SSC/ 0.1 % SDS for 20 minutes each time at 60°C. The filters are subjected to an autoradiography overnight. The colonies corresponding to the positive clones (spots obtained) are isolated and subjected to a second screening by a new plating at low density followed by hybridization: 6 clones are thus obtained (from 144 000) which are then sequenced using an ABI 377 device. Sequences are compiled using ABI software then analyzed using a GCG software package. One of the 6 clones is shown to contain the complete coding sequence corresponding to the probe used: this gene is called CaFL024 and this sequence called SEQ ID NO 9.

CaFL024 has 49.1 % of nucleotides identical to YFL024c of *S. cerevisiae*.

There are 2 CTG codons in CaFL024. The protein derived from the gene CaFL024 (SEQ ID No. 9) namely SEQ ID No. 10 (PCaFL024) has 51.8 % similarity in amino acids and 44.0 % identity in amino acids with the protein derived from YFL024c.

EXAMPLE 5: Cloning and sequencing of the gene CaNL260

The operation is carried out as in Example 4 starting from preliminary sequences of the genome of *Candida albicans* on the Stanford Internet site (http://candida.standford.edu/). One of these sequences has an homology with the gene YNl260c of *S. cerevisiae*. Two oligonucleotides were chosen in this sequence namely:
5' AGATAATGTATTAAATTTAG 3' called SEQ ID No. 29
and 5'CTCTTAATTTATTTCTTGCC 3' called SEQ ID No. 30.

These two oligonucleotides are used to amplify the fragment of *C. albicans*. After cloning, a so-called probe sequence of CaNL260 of 326 base pairs close to the expected sequence was obtained: the probe of CaNL260 is called SEQ ID No. 19. The protein derived from the probe of CaNL260 (SEQ ID No. 19) was compared to that of YNL260c which demonstrates a similarity of 56.7 % and an identity of 40.3 % between these two AA sequences: this comparison is represented in

Figure 5.

The fragment of 326 base pairs of *C. albicans* was used as probe for screening the gene bank of *C. albicans* prepared by partial digestion of the genomic DNA of *C. albicans* proceeding as in Example 4.

The prehybridization and hybridization are carried out as indicated in Example 4, 2 positive clones are obtained (from 40 000). The sequencing and analysis of the sequences obtained are carried out as indicated in Example 4, and a clone is thus obtained shown to contain the complete coding sequence corresponding to the probe used: this gene is called CaNL260 and this sequence is called SEQ ID No. 11.

CaNL260 has 47.6 % of nucleotides identical to YNL260c of *S. cerevisiae*.

The protein derived from the gene CaNL260 (SEQ ID No. 11) namely SEQ ID No. 12 (PCaNL260) has 50.7 % similarity in amino acids and 32.6 % identity in amino acids with the protein derived from YNL260c.

There is no CTG codon in CaNL260.

EXAMPLE 6: Cloning and sequencing of the gene CaDR361

The operation is carried out as in Example 4 starting from preliminary sequences of the genome of *Candida albicans*: The Stanford Internet site (http://candida.standford.edu/) allows direct access to the preliminary sequences of the genome of *Candida albicans*.

One of these sequences has an homology with the gene YDR361c of *S. cerevisiae*. Two oligonucleotides were chosen in this sequence namely:

5' CCTCAAATTGATTTCCATGC 3' called SEQ ID No. 31

and 5'GTGGAATCACTTCAACTGGC 3' called SEQ ID No. 32.

These two oligonucleotides are used to amplify the fragment of *C. albicans*. After cloning, a so-called probe sequence of CaDR361 of 374 base pairs close to the expected sequence was obtained: the probe of CaDR361 is called SEQ ID No. 20. The protein derived from the probe of CaDR361 (SEQ ID No. 20) was compared to that of YDR361c which demonstrates a similarity of 52.4 % and an identity of 40.0 % between these two AA sequences: this comparison is represented in

Figure 6.

The fragment of 374 base pairs of *C. albicans* was used as probe for screening the gene bank of *C. albicans* prepared by partial digestion of the genomic DNA of *C. albicans* by Sau11/A and cloning in the vector YEP 24 (selection marker Trp) at the Bam HI restriction site.

The prehybridization and hybridization are carried out as indicated in Example 4, 4 positive clones are obtained (from 40 000). The sequencing and analysis of the sequences obtained are carried out as indicated in Example 4, and thus a clone is obtained which is shown to contain the complete coding sequence corresponding to the probe used: this gene is called CaDR361 and this sequence called SEQ ID No. 13.

CaDR361 has 53.9 % of nucleotides identical to YDR361c of *S. cerevisiae*.

CaDR361 there is no CTG codon in CaDR361.

CLAIMS

1) Isolated polynucleotides each containing a nucleotide sequence chosen from the following group:

a) a polynucleotide having at least 50 % or at least 60 % and preferably at least 70 % identity with a polynucleotide coding for a polypeptide having the same function and having an amino acid sequence homologous with a sequence chosen from SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14,

b) a complementary polynucleotide of polynucleotide a)

c) a polynucleotide comprising at least 15 consecutive bases of the polynucleotide defined in a) and b).

2) Polynucleotides according to claim 1 such that these polynucleotides are of DNA.

3) Polynucleotides according to claim 1 such that these polynucleotides are of RNA.

4) Polynucleotides as defined in claim 2 each comprising a nucleotide sequence chosen from SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11 and SEQ ID No. 13.

5) DNA sequences as defined in claims 1, 2 and 4 characterized in that these DNA sequences are those of the genes coding respectively for the proteins of Candida albicans (having the same functions as the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361) and each containing a nucleotide sequence chosen from SEQ ID No. 1, SEQ ID No. 3, SEQ ID No. 5, SEQ ID No. 7, SEQ ID No. 9, SEQ ID No. 11 and SEQ ID No. 13.

6) DNA sequences of genes according to claim 5 each coding for an amino acid sequence chosen from SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14.

7) DNA sequences coding for the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 according to claims 5 and 6 as well as the DNA sequences which hybridize with these and/or have significant homologies with

these sequences or the fragments of these and code for proteins having the same functions.

8) DNA sequences according to claims 5 to 7 comprising modifications introduced by suppression, insertion and/or substitution of at least one nucleotide coding for the proteins having the same activities as the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361.

9) DNA sequences according to one of claims 5 to 8 as well as the DNA sequences which have an homology of nucleotide sequence of at least 50 % or at least 60 % and preferably at least 70 % with said DNA sequences.

10) DNA sequences according to one of claims 5 to 9 as well as the DNA sequences which code for the proteins with similar functions the respective AA sequences of which have an homology of at least 40 % and in particular of 45 % or of at least 50 %, rather at least 60 % and preferably at least 70 % with the AA sequences coded by said DNA sequences.

11) Polypeptides each having an amino acid sequence chosen from SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14 coded by the DNA sequences according to one of claims 5 to 10 and the analogues of these polypeptides.

12) Process for the preparation of recombinant proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 having respectively the amino acid sequences SEQ ID No. 2, SEQ ID No. 4, SEQ ID No. 6, SEQ ID No. 8, SEQ ID No. 10, SEQ ID No. 12 and SEQ ID No. 14 comprising, for the preparation of each of these proteins, the expression in an appropriate host of the DNA sequence coding for this protein according to one of claims 5 to 10 then the isolation and purification of said recombinant protein.

13) Expression vectors each containing one of the DNA sequences according to one of claims 5 to 10.

14) Host cell transformed with a vector according to claim 13.

15) Process as defined in claim 12 in which the host cell is DH5 alpha E. coli or XL1-Blue E. coli.

16) Process as defined in claim 13 in which the host cell is

Saccharomyces cerevisae.

17) One or more of the plasmids deposited at the CNCM under the numbers I-2214, I-2215, I-2216, I-2217, I-2211, I-2212 and I-2213.

18) Screening process for antifungal products characterized in that it comprises a stage where the activity of one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361, as defined in claim 11 is measured, in the presence of each of the products of which one wishes to determine the antifungal properties and the products having an inhibitory effect on this activity are selected.

19) Use of a product selected by the process according to claim 18 to obtain an antifungal agent.

20) Use of the genes of Candida albicans or of the proteins coded by these genes according to one of claims 5 to 11 for the selection of products having antifungal properties according to claim 19 as inhibitors of the proteins of Candida albicans coded by these genes.

21) Pharmaceutical compositions containing as active ingredient at least one inhibitor of the proteins of Candida albicans as defined in claim 20.

22) Use of the compositions as defined in claim 21 as antifungal agents.

23) Use of a polypeptide as defined in claim 11 or a fragment of this polypeptide having the same function for the preparation of a medicament intended to induce an immunological response in a mammal by inoculation of this medicament producing an antibody which allows said mammal to be protected against the disease.

24) Antibody directed against a polypeptide as defined in claim 11 or a fragment of this polypeptide having the same function.

25) Antibody as defined in claim 24 directed against any one of the proteins PCaDR472, PCaDR489, 1PCaDR527, 2PCaDR527, PCaFL024, PCaNL260, PCaDR361 or a fragment of these proteins.

26) Use of any one of the genes CaDR472, CaDR489, 1CaDR527, 2CaDR527, CaFL024, CaNL260 and CaDR361 or of any one of the proteins coded by these genes according to one of claims 5 to

11 for the preparation of compositions which can be used for the diagnosis or treatment of diseases caused by the pathogenic yeast Candida albicans.

27) Kit for the diagnosis of fungal infections comprising a DNA sequence as defined in one of claims 5 to 10 or a sequence having a similar function or a functional fragment of this sequence, the polypeptide coded by this sequence or a polypeptide fragment having the same function or an antibody directed against such polypeptide coded by this DNA sequence or against a fragment of this polypeptide.

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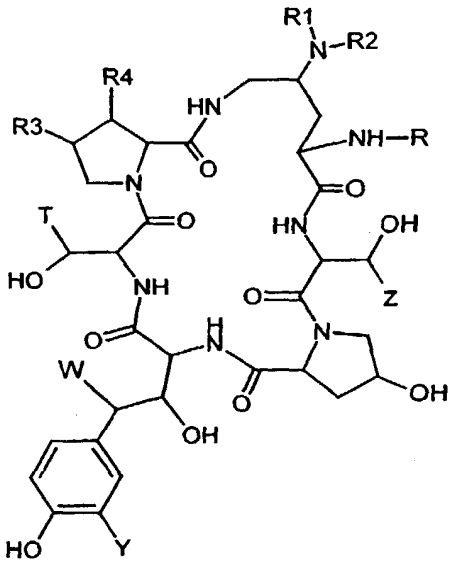
[Suite sur la page suivante]

(54) Title: NOVEL ECHINOCANDIN DERIVATIVES, METHOD FOR PREPARING SAME AND USE AS ANTIFUNGAL AGENTS

(54) Titre: NOUVEAUX DERIVES DE L'ECHINOCANDINE, LEUR PROCEDE DE PREPARATION ET LEUR APPLICATION COMME ANTIFONGIQUES



(I)

(57) Abstract: The invention concerns compounds of formula (I) wherein: either R_1 and R_2 = H, OH, alkyl optionally substituted, or NR_1 forms with the carbon bearing NR_1R_2 a double bond and R_2 is XRa, X being O, NH or N-alkyl and Ra being H, alkyl optionally substituted, or R_2 is e-N = C(-N-d)-N(f)-g; R_3 = H, OH, CH_3; R_4 = H, OH; R = chain containing up to 30 carbon atoms, optionally containing one or several heteroatoms, one or several heterocycles; T = H, CH_3, CH_2CONH_2, $CH_2C{\equiv}N$, $(CH_2)_2NH_2$, $(CH_2)_2Nalk^+X^-$; Y = H, OH, halogen, OSO_3H; W = H, OH; Z = H or CH_3. The products have antifungal properties.

[Suite sur la page suivante]

WO 00/75178 A1

CaDR472w x YDR472w probe comparison translation:

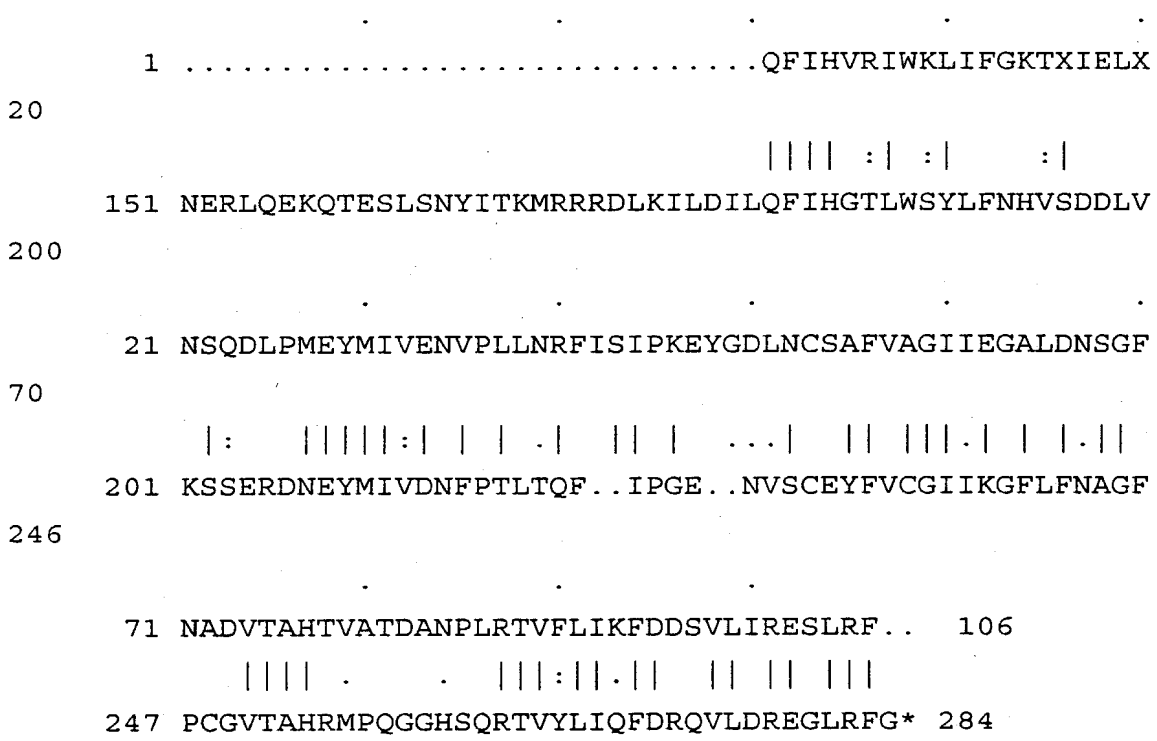


FIGURE 1

CaDR489 x YDR489w probe comparison translation:

```
                .         .         .         .         .
      1 ..........................FMFGDSERLNYIVRLYIRTRLSK
23
                                    | : |||:::| ||| ||||
    101 ISMGFLDMQNASNANPPMPNESKLPLLCMETELERLKFVIRSYIRCRLSK
150
                .         .         .         .         .
     24 LNKFTIFYINESSQNDN.......LLSKEERDYIHKYFQILTQLYNNCFL
66
        :.||.: |:: .:.:|        ||||:|  |  :  |  .| |.  |
    151 IDKFSL.YLRQLNEDENSLISLTDLLSKDEIKYHDTHSLIWLKLVNDSIL
199
                .         .         .         .         .
     67 KKLPQMLTYLDDTSGGQSMIVEPDLDQPVFIK..................
98
        |:|: | :.|| |  .|| ||| ..  |||
    200 KYMPEELQAINDTEGSVNMIDEPDWNKFVFIHVNGPPDGKWNEDPLLQEN
249
```

FIGURE 2

CaDR527 x YDR527w probe comparison translation:

```
                                    .         .         .          .
       1 ....................................ISDMRFGFKGDLIE
14
                                                :|: || | |||:
     251 DKLHEKYFPDLPKEVDKLKWMQPVQQKTDKNYIIEDVSECRFDFNGDLV.
299
                 .         .         .         .          .
      15 LAPVGDAPKDSSSDIRTHMGLHHHSETPHMAGYTLGELAHLARSTLAGQR
64
                |     |   | ||||||:.|:||||: || ||||||   ||
     300 .......PPTRQIDSTIHSGLHHHSDSPELAGYTIVELEHLARSTFPSQR
342
                 .         .         .         .          .
      65 CLSIQTLGRIFHKLGLHKYSILPNQLNDQSFTDESKLSLDFEDRCGT**T
114
           |:.|||||||:|||   |  | ::.  .::: :| .  |:  .
     343 CIAIQTLGRILYKLGQKSYYQLVPEIDADTYKEDGSIS.NVMDKIYSMF.
390
                 .         .         .         .          .
     115 NYESLKQ*QRQLMEKR.................................
130
           :::|    ...|
     391 .WDLIKDG..KVIESLEISSDEKFTRNLSVRNYAIDALWLWKQGGGDFRT
437
```

FIGURE 3

CaFL024 x YFL024c probe comparison translation:

```
                .         .         .         .         .
      1 ..................IPTPDASRIWPEAHKYYKDQKFKQPETYIK
30
                           |||||||  | |  |:|    |.:  .|||
    101 EVHLHRILQMGSGHTKHKDYIPTPDASMTWNEYDKFYTG.SFQETTSYIK
149
                .         .         .         .         .
     31 FSATVEDTVGVEYNMDEVDEKFYRETLCKYYPKKKNKSDENNRKCTELEF
80
        |||||||  |  ||||| || |  | .       |  ||       || ||
    150 FSATVEDCCGTNYNMDERDETFLNEQV......NKGSSD....ILTEDEF
189
                .         .         .         .         .
     81 ETICDKLEKTIEARQPFLSMDPSNILSYEEL...................
111
        |:|   |  |  ||||||||| .|||:|||
    190 EILCSSFEHAIHERQPFLSMDPESILSFEELKPTLIKSDMADFNLRNQLN
239
```

FIGURE 4

CaNL260c.x YNL260c. probe comparison translation:

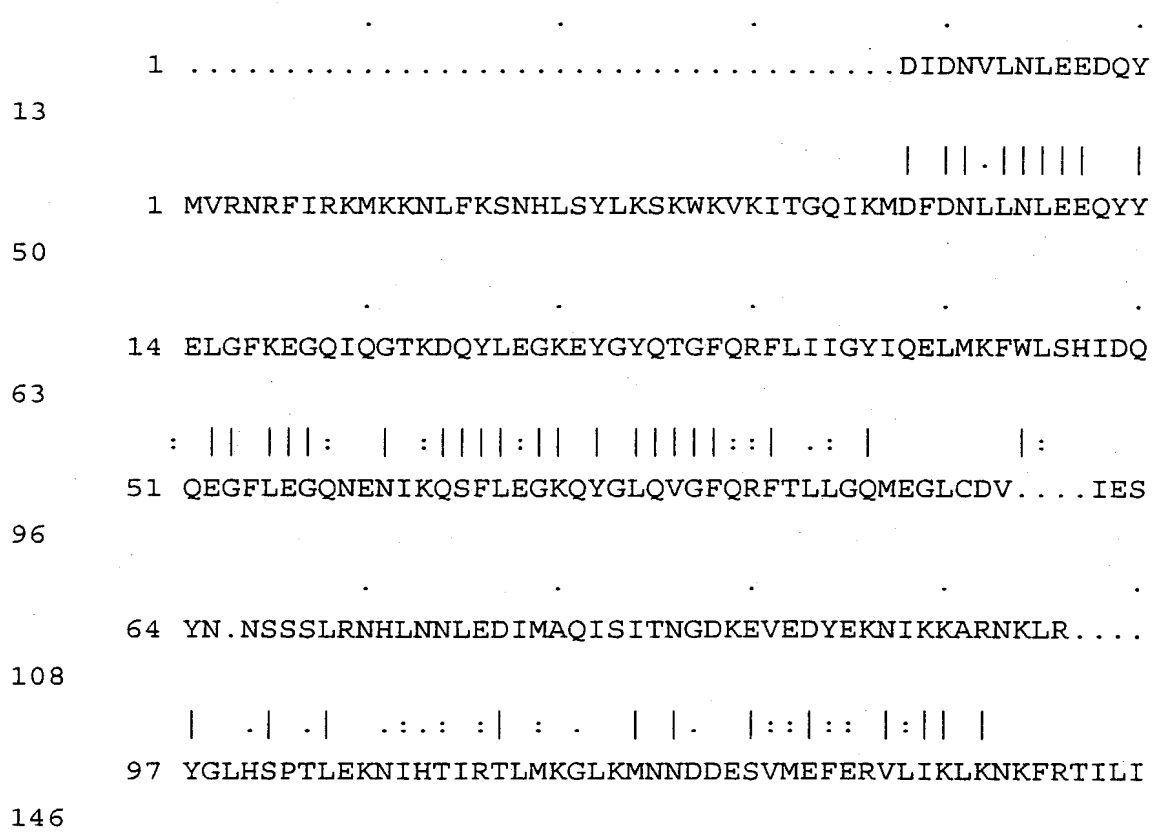


FIGURE 5

CaDR361 x YDR361c probe comparison translation:

```
                .         .         .         .         .
       1 ............LKLISMLLRIFKTLFG.DDNGEFNLSEIADLILRENS
36
                      :  |||     ||| :.    ||:|||||   |
      51 IDFDFFGGNPEVDFHALKNLLR...QLFGPQESTRIQLSSLADLIL..GS
95
                .         .         .         .         .
      37 VGTSIKTEGMESDPFAILSVINLTNNLNVAVIKQLIEYILNKTKSKTEFN
86
                |.|||:| ||||:  ||:.   |         |:|:    |     .
      96 PTTTIKTDGKESDPYCFLSFVDFKAN.......HLSDYVKYLQKVDMRLS
138
                .         .         .         .         .
      87 IILKKLLTNQNDTTRDRKFKTGLIISERFINMPVEVIP............
124
                |:: .  |           |::||| |||| ||:|
     139 TFFKTMIDSGNK.......NCALVLSERLINMPPEVVPPLYKITLEDVAT
181
```

FIGURE 6

Please type a plus sign (+) inside this box →

PTO/SB/01 (8-98)
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Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
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DECLARATION FOR UTILITY OR DESIGN PATENT APPLICATION

☒ Declaration Submitted with Initial Filing ☐ Declaration Submitted after Initial Filing

Attorney Docket Number	146.1374
First Named Inventor	J.L. LALANNE et al
COMPLETE IF KNOWN	
Application Number	PCT/FR00/01567
Filing Date	June 8, 2000
Group Art Unit	
Examiner Name	

As a below named inventor, I hereby declare that:

My residence, post office address, and citizenship are as stated below next to my name.

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled :

NOVEL CANDIDA ALBICANS GENES AND PROTEINS CODED BY THESE GENES

(Title of the Invention)

the specification of which

☐ is attached hereto

OR

☒ was filed on (MM/DD/YYYY) June 8, 2000 as United States Application Number or PCT International Application Number PCT/FR00/01567 and was amended on (MM/DD/YYYY) _____ (if applicable).

I hereby state that I have reviewed and understand the contents of the above identified specification, including the claims, as amended by any amendment specifically referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in Title 37 Code of Federal Regulations, §1.56.

I hereby claim foreign priority benefits under Title 35, United States Code §119 (a)-(d) or §365(b) of any foreign application(s) for patent or inventor's certificate, or §365 (a) of any PCT international application which designated at least one country other than the United States of America, listed below and have also identified below, by checking the box, any foreign application for patent or inventor's certificate, or of any PCT international application having a filing date before that of the application on which priority is claimed.

Prior Foreign Application Number(s)	Country	Foreign Filing Date (MM/DD/YYYY)	Priority Not Claimed	Certified Copy Attached? YES	Certified Copy Attached? NO
99/07250	France	6/9/99	☐	☐	☐
			☐	☐	☐
			☐	☐	☐
			☐	☐	☐
			☐	☐	☐
			☐	☐	☐

☐ Additional foreign application numbers are listed on a supplemental priority sheet attached hereto:

I hereby claim the benefit under Title 35, United States Code § 119(e) of any United States provisional application(s) listed below

Application Number(s)	Filing Date (MM/DD/YYYY)

☐ Additional provisional application numbers are listed on a supplemental priority sheet attached hereto

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DECLARATION

I hereby claim the benefit under Title 35, United States Code §120 of any United States application(s), or §365(c) of any PCT international application designating the United States of America, listed below and, insofar as the subject matter of each of the claims of this application is not disclosed in the prior United States or PCT International application in the manner provided by the first paragraph of Title 35, United States Code §112 I acknowledge the duty to disclose information which is material to patentability as defined in Title 37, Code of Federal Regulations §1.56 which became available between the filing date of the prior application and the national or PCT international filing date of this application.

U.S. Parent Application Number	PCT Parent Number	Parent Filing Date (MM/DD/YYYY)	Parent Patent Number (if applicable)

☐ Additional U.S. or PCT international application numbers are listed on a supplemental priority sheet attached hereto.

As a named inventor, I hereby appoint the following registered practitioner(s) to prosecute this application and to transact all business in the Patent and Trademark Office connected therewith:

Name	Registration Number	Name	Registration Number
Charles A. Muserlian Jordan B. Bierman Donald C. Lucas Bierman, Muserlian and Lucas	~~19,683~~ ~~18,629~~ ~~31,275~~ 10,010	(4)	

☐ Additional registered practitioner(s) named on a supplemental sheet attached hereto.

Direct all correspondence to:

Name	Bierman, Muserlian and Lucas
Address	
Address	600 Third Avenue
City	New York
State	New York
ZIP	10016-
Country	U.S.A.
Telephone	(212) 661-8000
Fax	(212) 661-8002

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Name of Sole or First Inventor: ☐ A petition has been filed for this unsigned inventor

Given Name	Middle Initial	Family Name	Suffix e.g. Jr.
JEAN	L	LALANNE	

Inventor's Signature: [signature] Date: December 17th 2001

Residence: City	State	Country	Citizenship
Fontenay sous Bois		France FRX	FR.

Post Office Address	
Post Office Address	110, avenue du Marechal
City	Fontenay sous Bois
State	
Zip	F-94120
Country	France

☒ Additional inventors are being named on supplemental sheet(s) attached hereto

Please type a plus sign (+) inside this box → [+] 146.1374

PTO/SB/01 (8-96)
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DECLARATION	ADDITIONAL INVENTOR(S) Supplemental Sheet

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name	CORINNE	Middle Initial		Family Name	ROCHER
Inventor's Signature	[signature]			Date	December 13, 2001
Residence: City	Paris	State		Country	France FRX
Citizenship	FR				
Post Office Address					
Post Office Address	3, rue Elisa Lemonnier				
City	Paris	State		Zip	F-75012
Country	France				

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name	
Suffix e.g. Jr.					
Inventor's Signature				Date	
Residence: City		State		Country	
Citizenship					
Post Office Address					
Post Office Address					
City		State		Zip	
Country					

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name	
Suffix e.g. Jr.					
Inventor's Signature				Date	
Residence: City		State		Country	
Citizenship					
Post Office Address					
Post Office Address					
City		State		Zip	
Country					

Name of Additional Joint Inventor, if any: ☐ A petition has been filed for this unsigned inventor

Given Name		Middle Initial		Family Name	
Suffix e.g. Jr.					
Inventor's Signature				Date	
Residence: City		State		Country	
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Post Office Address					
Post Office Address					
City		State		Zip	
Country					

☐ Additional inventors are being named on supplemental sheet(s) attached hereto

(January 1997)

SEQUENCE LISTING

<110> LALANNE, JEAN L
ROCHER, CORINNE

<120> Novel genes of Candida albicans and the proteins coded by these genes

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<140> 09/980,054
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  1               5                  10                  15

cta act ata aat gat gta tca aaa tca gga ttt gga tac aat ccg tcc   96
Leu Thr Ile Asn Asp Val Ser Lys Ser Gly Phe Gly Tyr Asn Pro Ser
             20                  25                  30

ata gga cca ata tca aat act att acc cta gaa tct tca ctg gta tta   144
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         35                  40                  45
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50 55 60

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Tyr Asp Arg Asn Ile Ile Thr Lys Lys Pro His Glu Ile Asn Leu Ser
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Ser Leu Ser Phe Leu Phe Cys Glu Ile Ile Ser Trp Ala His Ser Asn
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tcc aaa ggc att caa gat tta gaa aat cgt tta aac gga tta ggt tat 336
Ser Lys Gly Ile Gln Asp Leu Glu Asn Arg Leu Asn Gly Leu Gly Tyr
100 105 110

caa ata ggt caa cga tat ctc gaa ttg tgt aaa ata aga gaa ggt ttt 384
Gln Ile Gly Gln Arg Tyr Leu Glu Leu Cys Lys Ile Arg Glu Gly Phe
115 120 125

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Ser Gly Phe Asn Ala Asp Val Thr Ala His Thr Val Ala Thr Asp Ala
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Ser Lys Gly Ile Gln Asp Leu Glu Asn Arg Leu Asn Gly Leu Gly Tyr
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His Gly Pro Phe Trp Lys Leu Ile Phe Gly Lys Thr Ala Asn Glu Leu
145 150 155 160
Glu Lys Ser Gln Asp Leu Pro Asn Glu Tyr Met Ile Val Glu Asn Val
165 170 175
Pro Leu Leu Asn Arg Phe Ile Ser Ile Pro Lys Glu Tyr Gly Asp Leu
180 185 190
Asn Cys Ser Ala Phe Val Ala Gly Ile Ile Glu Gly Ala Leu Asp Asn
195 200 205
Ser Gly Phe Asn Ala Asp Val Thr Ala His Thr Val Ala Thr Asp Ala
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  1               5                  10                  15

gaa aag att agc agt aaa aca tcg tct atc aac tta tat caa gac ttg   96
Glu Lys Ile Ser Ser Lys Thr Ser Ser Ile Asn Leu Tyr Gln Asp Leu
             20                  25                  30

cta aga gct atg atc aac gaa cgt atg gct ccg gaa tta ttg cca tac   144
Leu Arg Ala Met Ile Asn Glu Arg Met Ala Pro Glu Leu Leu Pro Tyr
         35                  40                  45

aaa caa gat tta atg tcc act gtt tta aca atg atg tct aac caa caa   192
Lys Gln Asp Leu Met Ser Thr Val Leu Thr Met Met Ser Asn Gln Gln
     50                  55                  60

caa tat tta tta gaa tct cac gaa tat ggt gat atg aat ggc gac agt   240
Gln Tyr Leu Leu Glu Ser His Glu Tyr Gly Asp Met Asn Gly Asp Ser
 65                  70                  75                  80

ggt gta tta tcc gga gac ttt aaa tta caa cta atg att atc gaa act   288
Gly Val Leu Ser Gly Asp Phe Lys Leu Gln Leu Met Ile Ile Glu Thr
                 85                  90                  95

gat tta gag cgt ctc aac tat att gtt cga tta tac ata cga act cga   336
Asp Leu Glu Arg Leu Asn Tyr Ile Val Arg Leu Tyr Ile Arg Thr Arg
            100                 105                 110

ttg agt aag ttg aat aaa ttt act att ttt tac atc aat gaa agc agt   384
Leu Ser Lys Leu Asn Lys Phe Thr Ile Phe Tyr Ile Asn Glu Ser Ser
        115                 120                 125

caa aat gat aat tta ttg tcc aaa gag gaa aga gat tat ata cac aaa   432
Gln Asn Asp Asn Leu Leu Ser Lys Glu Glu Arg Asp Tyr Ile His Lys
    130                 135                 140
```

```
tat ttc cag att ttg act caa tta tat aac aac tgt ttc ctc aaa aaa   480
Tyr Phe Gln Ile Leu Thr Gln Leu Tyr Asn Asn Cys Phe Leu Lys Lys
145                 150                 155                 160

cta cca caa atg ttg acc tat ttg gat gac acc agt ggt gga caa tca   528
Leu Pro Gln Met Leu Thr Tyr Leu Asp Asp Thr Ser Gly Gly Gln Ser
                165                 170                 175

atg atc gtt gag cca gat tta gac cag cct gtg ttt atc aaa tgt acc   576
Met Ile Val Glu Pro Asp Leu Asp Gln Pro Val Phe Ile Lys Cys Thr
            180                 185                 190

ctg gaa gtc cca ata tta cta gat tac gac ggt gct aca gag ata gat   624
Leu Glu Val Pro Ile Leu Leu Asp Tyr Asp Gly Ala Thr Glu Ile Asp
        195                 200                 205

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Leu Glu Leu Ile Lys Lys Gly Val Tyr Val Val Lys Tyr Ser Leu Val
    210                 215                 220

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Lys Arg Tyr Ile Asp Ile Gly Asp Val Val Leu Ile
225                 230                 235
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<210> 4
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Glu Lys Ile Ser Ser Lys Thr Ser Ser Ile Asn Leu Tyr Gln Asp Leu
             20                  25                  30
Leu Arg Ala Met Ile Asn Glu Arg Met Ala Pro Glu Leu Leu Pro Tyr
         35                  40                  45
Lys Gln Asp Leu Met Ser Thr Val Leu Thr Met Met Ser Asn Gln Gln
     50                  55                  60
Gln Tyr Leu Leu Glu Ser His Glu Tyr Gly Asp Met Asn Gly Asp Ser
 65                  70                  75                  80
Gly Val Leu Ser Gly Asp Phe Lys Leu Gln Leu Met Ile Ile Glu Thr
                 85                  90                  95
Asp Leu Glu Arg Leu Asn Tyr Ile Val Arg Leu Tyr Ile Arg Thr Arg
            100                 105                 110
Leu Ser Lys Leu Asn Lys Phe Thr Ile Phe Tyr Ile Asn Glu Ser Ser
        115                 120                 125
```

Gln Asn Asp Asn Leu Leu Ser Lys Glu Glu Arg Asp Tyr Ile His Lys
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Leu Lys Glu Lys Lys Val Ser Arg Trp Arg Gln Lys Gln Gln Gln Glu
35 40 45

cag agc aca act tcc cca aaa act act gaa atc cgt tca gag gct tcc 192
Gln Ser Thr Thr Ser Pro Lys Thr Thr Glu Ile Arg Ser Glu Ala Ser
50 55 60

aaa att cac caa gaa aat atc gag aag atg gct caa atg tca gag gaa 240
Lys Ile His Gln Glu Asn Ile Glu Lys Met Ala Gln Met Ser Glu Glu
65 70 75 80

gag att ttg caa gag cgt gag gag tta cta aag ggt tta gat cct aaa 288

```
Glu Ile Leu Gln Glu Arg Glu Glu Leu Leu Lys Gly Leu Asp Pro Lys
                  85                  90                  95

tta att gaa agt ttg att ggt aga tcc aag aaa agg gaa gca aca gac   336
Leu Ile Glu Ser Leu Ile Gly Arg Ser Lys Lys Arg Glu Ala Thr Asp
            100                 105                 110

cat gaa cac aat gga cat gct cat gaa cat gca gag gga tac cat gga   384
His Glu His Asn Gly His Ala His Glu His Ala Glu Gly Tyr His Gly
        115                 120                 125

tgg att gga tca atg aaa act tct gaa gga tta aca gat tta tct caa   432
Trp Ile Gly Ser Met Lys Thr Ser Glu Gly Leu Thr Asp Leu Ser Gln
    130                 135                 140

tta gat aag gaa gat gtg gac cgt gca ttg ggt ata agt tca tta tcc   480
Leu Asp Lys Glu Asp Val Asp Arg Ala Leu Gly Ile Ser Ser Leu Ser
145                 150                 155                 160

tta tct gaa cct gag ggt ggc agt aat acg aaa aaa gtc gct ttc gac   528
Leu Ser Glu Pro Glu Gly Gly Ser Asn Thr Lys Lys Val Ala Phe Asp
                165                 170                 175

gat aat atc aag acg gtt aaa ttt gaa gat ttg gat gat gga att gaa   576
Asp Asn Ile Lys Thr Val Lys Phe Glu Asp Leu Asp Asp Gly Ile Glu
            180                 185                 190

ttg gat cca aat gga tgg gag gac gtt act gat gtc aat gaa tta gtt   624
Leu Asp Pro Asn Gly Trp Glu Asp Val Thr Asp Val Asn Glu Leu Val
        195                 200                 205

cct aat aat gat cac att gca cct gac gat tac cag att aat cct gat   672
Pro Asn Asn Asp His Ile Ala Pro Asp Asp Tyr Gln Ile Asn Pro Asp
    210                 215                 220

agc gat gaa gaa gga ttg aat aat act gtt cat ttt aca aaa ccc aaa   720
Ser Asp Glu Glu Gly Leu Asn Asn Thr Val His Phe Thr Lys Pro Lys
225                 230                 235                 240

cag cca gat ttg gat ata aat gat ccc gat ttc ttt gat aag cta cat   768
Gln Pro Asp Leu Asp Ile Asn Asp Pro Asp Phe Phe Asp Lys Leu His
                245                 250                 255

gag aaa tac tat cct gat ttg cct aaa gaa aca gaa aag ttg tca tgg   816
Glu Lys Tyr Tyr Pro Asp Leu Pro Lys Glu Thr Glu Lys Leu Ser Trp
            260                 265                 270

atg aca cag cca atg cca aaa caa ttg tct acc gtt tat gaa tca ata   864
```

```
Met Thr Gln Pro Met Pro Lys Gln Leu Ser Thr Val Tyr Glu Ser Ile
        275                 280                 285

tct gat atg aga ttt gac ttt aaa gga gat tta att gaa ttg ggt cca   912
Ser Asp Met Arg Phe Asp Phe Lys Gly Asp Leu Ile Glu Leu Gly Pro
    290                 295                 300

gag gga gaa gaa cca aaa gat agt tca tcc gaa ata cct act tat atg   960
Glu Gly Glu Glu Pro Lys Asp Ser Ser Ser Glu Ile Pro Thr Tyr Met
305                 310                 315                 320

gga ctt cat cat cat tcg gag aac cca cat atg gca ggt tat aca ttg   1008
Gly Leu His His His Ser Glu Asn Pro His Met Ala Gly Tyr Thr Leu
                325                 330                 335

ggt gag ttg gca cat tta gcc aga tcg act tta gct gga caa aga tgc   1056
Gly Glu Leu Ala His Leu Ala Arg Ser Thr Leu Ala Gly Gln Arg Cys
            340                 345                 350

ttg agc att caa aca tta ggg aga atc tta cat aaa ttg gga tta cat   1104
Leu Ser Ile Gln Thr Leu Gly Arg Ile Leu His Lys Leu Gly Leu His
        355                 360                 365

aaa tac agt ata cta cca aaa aca gac tca gat gat cag agt ttt aca   1152
Lys Tyr Ser Ile Leu Pro Lys Thr Asp Ser Asp Asp Gln Ser Phe Thr
    370                 375                 380

gat gaa atc aaa caa cta tca ctt gac ttt gaa gat atg atg tgg gac   1200
Asp Glu Ile Lys Gln Leu Ser Leu Asp Phe Glu Asp Met Met Trp Asp
385                 390                 395                 400

ttg ata gac caa tta cga atc att gaa aca ata aca gag gca gct gat   1248
Leu Ile Asp Gln Leu Arg Ile Ile Glu Thr Ile Thr Glu Ala Ala Asp
                405                 410                 415

gaa aaa aag acc aga aac tta tct gtc aga aat tat gca ata gag gca   1296
Glu Lys Lys Thr Arg Asn Leu Ser Val Arg Asn Tyr Ala Ile Glu Ala
            420                 425                 430

ttg tgg tta tat aga act gga ggt gga aga cca gag ata act aaa caa   1344
Leu Trp Leu Tyr Arg Thr Gly Gly Gly Arg Pro Glu Ile Thr Lys Gln
        435                 440                 445

acc gaa gag gat ttg ata gca caa gca gtt cag aaa taa               1383
Thr Glu Glu Asp Leu Ile Ala Gln Ala Val Gln Lys
    450                 455                 460
```

<210> 6
<211> 460
<212> PRT
<213> Candida albicans

<400> 6
Met Asp Phe Ile Gly Glu Ile Ile Glu His Glu Thr Glu Ala Pro Lys
1 5 10 15
Glu Pro Thr Pro Lys Pro Thr Ile Gly Gly Phe Pro Glu Leu Lys Lys
20 25 30
Leu Lys Glu Lys Lys Val Ser Arg Trp Arg Gln Lys Gln Gln Gln Glu
35 40 45
Gln Ser Thr Thr Ser Pro Lys Thr Thr Glu Ile Arg Ser Glu Ala Ser
50 55 60
Lys Ile His Gln Glu Asn Ile Glu Lys Met Ala Gln Met Ser Glu Glu
65 70 75 80
Glu Ile Leu Gln Glu Arg Glu Glu Leu Leu Lys Gly Leu Asp Pro Lys
85 90 95
Leu Ile Glu Ser Leu Ile Gly Arg Ser Lys Lys Arg Glu Ala Thr Asp
100 105 110
His Glu His Asn Gly His Ala His Glu His Ala Glu Gly Tyr His Gly
115 120 125
Trp Ile Gly Ser Met Lys Thr Ser Glu Gly Leu Thr Asp Leu Ser Gln
130 135 140
Leu Asp Lys Glu Asp Val Asp Arg Ala Leu Gly Ile Ser Ser Leu Ser
145 150 155 160
Leu Ser Glu Pro Glu Gly Gly Ser Asn Thr Lys Lys Val Ala Phe Asp
165 170 175
Asp Asn Ile Lys Thr Val Lys Phe Glu Asp Leu Asp Asp Gly Ile Glu
180 185 190
Leu Asp Pro Asn Gly Trp Glu Asp Val Thr Asp Val Asn Glu Leu Val
195 200 205
Pro Asn Asn Asp His Ile Ala Pro Asp Asp Tyr Gln Ile Asn Pro Asp
210 215 220
Ser Asp Glu Glu Gly Leu Asn Asn Thr Val His Phe Thr Lys Pro Lys
225 230 235 240
Gln Pro Asp Leu Asp Ile Asn Asp Pro Asp Phe Phe Asp Lys Leu His
245 250 255
Glu Lys Tyr Tyr Pro Asp Leu Pro Lys Glu Thr Glu Lys Leu Ser Trp
260 265 270
Met Thr Gln Pro Met Pro Lys Gln Leu Ser Thr Val Tyr Glu Ser Ile
275 280 285
Ser Asp Met Arg Phe Asp Phe Lys Gly Asp Leu Ile Glu Leu Gly Pro
290 295 300
Glu Gly Glu Glu Pro Lys Asp Ser Ser Ser Glu Ile Pro Thr Tyr Met
305 310 315 320
Gly Leu His His His Ser Glu Asn Pro His Met Ala Gly Tyr Thr Leu
325 330 335

```
Gly Glu Leu Ala His Leu Ala Arg Ser Thr Leu Ala Gly Gln Arg Cys
            340                 345                 350
Leu Ser Ile Gln Thr Leu Gly Arg Ile Leu His Lys Leu Gly Leu His
        355                 360                 365
Lys Tyr Ser Ile Leu Pro Lys Thr Asp Ser Asp Asp Gln Ser Phe Thr
    370                 375                 380
Asp Glu Ile Lys Gln Leu Ser Leu Asp Phe Glu Asp Met Met Trp Asp
385                 390                 395                 400
Leu Ile Asp Gln Leu Arg Ile Ile Glu Thr Ile Thr Glu Ala Ala Asp
                405                 410                 415
Glu Lys Lys Thr Arg Asn Leu Ser Val Arg Asn Tyr Ala Ile Glu Ala
            420                 425                 430
Leu Trp Leu Tyr Arg Thr Gly Gly Gly Arg Pro Glu Ile Thr Lys Gln
        435                 440                 445
Thr Glu Glu Asp Leu Ile Ala Gln Ala Val Gln Lys
    450                 455                 460
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<210> 7
<211> 1383
<212> DNA
<213> Candida albicans

<220>
<221> CDS
<222> (1)..(1380)

<400> 7

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atg gat ttc ata gga gag att ata gag cat gag aca gag gca cct aaa   48
Met Asp Phe Ile Gly Glu Ile Ile Glu His Glu Thr Glu Ala Pro Lys
  1               5                  10                  15

gaa cca acc cca aaa ccc aca att ggt gga ttc ccc gaa ctt aaa aaa   96
Glu Pro Thr Pro Lys Pro Thr Ile Gly Gly Phe Pro Glu Leu Lys Lys
             20                  25                  30

tta aaa gaa aag aaa gtc tca aga tgg agg caa aag caa caa cag gag   144
Leu Lys Glu Lys Lys Val Ser Arg Trp Arg Gln Lys Gln Gln Gln Glu
         35                  40                  45

cag agc aca act tcc cca aaa act act gaa atc cgt tca gag gct tcc   192
Gln Ser Thr Thr Ser Pro Lys Thr Thr Glu Ile Arg Ser Glu Ala Ser
     50                  55                  60

aaa att cac caa gaa aat atc gag aag atg gct caa atg tca gag gaa   240
Lys Ile His Gln Glu Asn Ile Glu Lys Met Ala Gln Met Ser Glu Glu
 65                  70                  75                  80
```

gag att ttg caa gag cgt gag gag tta cta aag ggt tta gac cct aaa 288
Glu Ile Leu Gln Glu Arg Glu Glu Leu Leu Lys Gly Leu Asp Pro Lys
85 90 95

tta att gaa agt ttg att ggt aga tcc aag aaa agg gaa gca aca gac 336
Leu Ile Glu Ser Leu Ile Gly Arg Ser Lys Lys Arg Glu Ala Thr Asp
100 105 110

cat gaa cac aat gga cat gct cat gaa cat gca gag gga tac cat gga 384
His Glu His Asn Gly His Ala His Glu His Ala Glu Gly Tyr His Gly
115 120 125

tgg att gga tca atg aaa act tct gaa gga tta aca gat tta tct caa 432
Trp Ile Gly Ser Met Lys Thr Ser Glu Gly Leu Thr Asp Leu Ser Gln
130 135 140

tta gat aag gaa gat gtg gac cgt gct ttg ggt ata agt tca tta tcc 480
Leu Asp Lys Glu Asp Val Asp Arg Ala Leu Gly Ile Ser Ser Leu Ser
145 150 155 160

tta tct gaa cct gag ggt ggc agc aat acg aaa aaa gtc gct ttc gac 528
Leu Ser Glu Pro Glu Gly Gly Ser Asn Thr Lys Lys Val Ala Phe Asp
165 170 175

gat aat atc aag acg gtt aaa ttt gaa gct ttg gat gat gaa att gaa 576
Asp Asn Ile Lys Thr Val Lys Phe Glu Ala Leu Asp Asp Glu Ile Glu
180 185 190

ttg gat cca aat gga tgg gag gac gtt act gat gtc aat gaa tta gtt 624
Leu Asp Pro Asn Gly Trp Glu Asp Val Thr Asp Val Asn Glu Leu Val
195 200 205

cct aat aat gat cac att gca cct gac gat tac cag att aat cct gat 672
Pro Asn Asn Asp His Ile Ala Pro Asp Asp Tyr Gln Ile Asn Pro Asp
210 215 220

agc gat gaa gaa gga ttg aat aat act gtt cat ttt aca aaa ccc aaa 720
Ser Asp Glu Glu Gly Leu Asn Asn Thr Val His Phe Thr Lys Pro Lys
225 230 235 240

cag cca gat ttg gat ata aat gat ccc gat ttc ttt gat aag cta cat 768
Gln Pro Asp Leu Asp Ile Asn Asp Pro Asp Phe Phe Asp Lys Leu His
245 250 255

gag aaa tac tat cct gat ttg cct aaa gaa aca gaa aag ttg tca tgg 816
Glu Lys Tyr Tyr Pro Asp Leu Pro Lys Glu Thr Glu Lys Leu Ser Trp
260 265 270

```
atg aca cag cca atg cca aaa caa ttg tct aca gtt tat gaa tca ata   864
Met Thr Gln Pro Met Pro Lys Gln Leu Ser Thr Val Tyr Glu Ser Ile
        275                 280                 285

tct gat atg aga ttt gac ttc aaa gga gat tta att gaa ttg agc gca   912
Ser Asp Met Arg Phe Asp Phe Lys Gly Asp Leu Ile Glu Leu Ser Ala
    290                 295                 300

gag gga gaa gaa cca aaa gat agt tca ttc gaa ata cct act tat atg   960
Glu Gly Glu Glu Pro Lys Asp Ser Ser Phe Glu Ile Pro Thr Tyr Met
305                 310                 315                 320

gga ctt cat cat cat tcg gag aac cca cat atg gca ggt tat aca ttg   1008
Gly Leu His His His Ser Glu Asn Pro His Met Ala Gly Tyr Thr Leu
                325                 330                 335

ggt gag ttg gca cat tta gcc aga tcg act tta gct gga caa aga tgc   1056
Gly Glu Leu Ala His Leu Ala Arg Ser Thr Leu Ala Gly Gln Arg Cys
            340                 345                 350

ttg agc att caa aca tta ggg aga ata tta cat aaa ttg gga tta cat   1104
Leu Ser Ile Gln Thr Leu Gly Arg Ile Leu His Lys Leu Gly Leu His
        355                 360                 365

aaa tac agt ata cta cca aaa aca gac tca gat gat cag agt ttt aca   1152
Lys Tyr Ser Ile Leu Pro Lys Thr Asp Ser Asp Asp Gln Ser Phe Thr
    370                 375                 380

gat gaa atc aaa caa cta tca ctt gac ttt gaa gat atg atg tgg gac   1200
Asp Glu Ile Lys Gln Leu Ser Leu Asp Phe Glu Asp Met Met Trp Asp
385                 390                 395                 400

ttg ata gac caa tta cga atc att gaa aca ata aca gag gca gct gat   1248
Leu Ile Asp Gln Leu Arg Ile Ile Glu Thr Ile Thr Glu Ala Ala Asp
                405                 410                 415

gaa aaa aag acc aga aac tta tct gtc aga aat tat gca ata gag gca   1296
Glu Lys Lys Thr Arg Asn Leu Ser Val Arg Asn Tyr Ala Ile Glu Ala
            420                 425                 430

ttg tgg tta tat aga act gga ggt gga aga cca gag ata act aaa caa   1344
Leu Trp Leu Tyr Arg Thr Gly Gly Gly Arg Pro Glu Ile Thr Lys Gln
        435                 440                 445

acc gaa gag gat ttg ata gca caa gca gtt cag aaa taa               1383
Thr Glu Glu Asp Leu Ile Ala Gln Ala Val Gln Lys
    450                 455                 460
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<210> 8
<211> 460
<212> PRT
<213> Candida albicans

<400> 8

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Met Asp Phe Ile Gly Glu Ile Ile Glu His Glu Thr Glu Ala Pro Lys
  1               5                  10                  15

Glu Pro Thr Pro Lys Pro Thr Ile Gly Gly Phe Pro Glu Leu Lys Lys
             20                  25                  30

Leu Lys Glu Lys Lys Val Ser Arg Trp Arg Gln Lys Gln Gln Gln Glu
         35                  40                  45

Gln Ser Thr Thr Ser Pro Lys Thr Thr Glu Ile Arg Ser Glu Ala Ser
     50                  55                  60

Lys Ile His Gln Glu Asn Ile Glu Lys Met Ala Gln Met Ser Glu Glu
 65                  70                  75                  80

Glu Ile Leu Gln Glu Arg Glu Glu Leu Leu Lys Gly Leu Asp Pro Lys
                 85                  90                  95

Leu Ile Glu Ser Leu Ile Gly Arg Ser Lys Lys Arg Glu Ala Thr Asp
            100                 105                 110

His Glu His Asn Gly His Ala His Glu His Ala Glu Gly Tyr His Gly
        115                 120                 125

Trp Ile Gly Ser Met Lys Thr Ser Glu Gly Leu Thr Asp Leu Ser Gln
    130                 135                 140

Leu Asp Lys Glu Asp Val Asp Arg Ala Leu Gly Ile Ser Ser Leu Ser
145                 150                 155                 160

Leu Ser Glu Pro Glu Gly Gly Ser Asn Thr Lys Lys Val Ala Phe Asp
                165                 170                 175

Asp Asn Ile Lys Thr Val Lys Phe Glu Ala Leu Asp Asp Glu Ile Glu
            180                 185                 190

Leu Asp Pro Asn Gly Trp Glu Asp Val Thr Asp Val Asn Glu Leu Val
        195                 200                 205

Pro Asn Asn Asp His Ile Ala Pro Asp Asp Tyr Gln Ile Asn Pro Asp
```

```
    210                 215                 220

Ser Asp Glu Glu Gly Leu Asn Asn Thr Val His Phe Thr Lys Pro Lys
225                 230                 235                 240

Gln Pro Asp Leu Asp Ile Asn Asp Pro Asp Phe Phe Asp Lys Leu His
                245                 250                 255

Glu Lys Tyr Tyr Pro Asp Leu Pro Lys Glu Thr Glu Lys Leu Ser Trp
            260                 265                 270

Met Thr Gln Pro Met Pro Lys Gln Leu Ser Thr Val Tyr Glu Ser Ile
        275                 280                 285

Ser Asp Met Arg Phe Asp Phe Lys Gly Asp Leu Ile Glu Leu Ser Ala
    290                 295                 300

Glu Gly Glu Glu Pro Lys Asp Ser Ser Phe Glu Ile Pro Thr Tyr Met
305                 310                 315                 320

Gly Leu His His His Ser Glu Asn Pro His Met Ala Gly Tyr Thr Leu
                325                 330                 335

Gly Glu Leu Ala His Leu Ala Arg Ser Thr Leu Ala Gly Gln Arg Cys
            340                 345                 350

Leu Ser Ile Gln Thr Leu Gly Arg Ile Leu His Lys Leu Gly Leu His
        355                 360                 365

Lys Tyr Ser Ile Leu Pro Lys Thr Asp Ser Asp Asp Gln Ser Phe Thr
    370                 375                 380

Asp Glu Ile Lys Gln Leu Ser Leu Asp Phe Glu Asp Met Met Trp Asp
385                 390                 395                 400

Leu Ile Asp Gln Leu Arg Ile Ile Glu Thr Ile Thr Glu Ala Ala Asp
                405                 410                 415

Glu Lys Lys Thr Arg Asn Leu Ser Val Arg Asn Tyr Ala Ile Glu Ala
            420                 425                 430

Leu Trp Leu Tyr Arg Thr Gly Gly Gly Arg Pro Glu Ile Thr Lys Gln
        435                 440                 445

Thr Glu Glu Asp Leu Ile Ala Gln Ala Val Gln Lys
    450                 455                 460
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<210> 9
<211> 2262
<212> DNA
<213> Candida albicans

<220>
<221> CDS
<222> (1)..(2262)

<220>
<221> modified_base
<222> (1093)..(1095)

<220>
<221> modified_base
<222> (1828)..(1830)

<400> 9

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atg gca gca gca cca cca cca cca gcg aaa aac cag ggt aag gca aaa   48
Met Ala Ala Ala Pro Pro Pro Pro Ala Lys Asn Gln Gly Lys Ala Lys
  1               5                  10                  15

cag cat gtt aca ggt gcc agg ttc cgt cag cga aaa atc tcg gta aag   96
Gln His Val Thr Gly Ala Arg Phe Arg Gln Arg Lys Ile Ser Val Lys
             20                  25                  30

cag ccc ttg act att tat aaa cag aga gac cta cct act cta gat agc   144
Gln Pro Leu Thr Ile Tyr Lys Gln Arg Asp Leu Pro Thr Leu Asp Ser
         35                  40                  45

aat gag tta gag cct agt caa gtc cat cat tta aat tct aat gcg tca   192
Asn Glu Leu Glu Pro Ser Gln Val His His Leu Asn Ser Asn Ala Ser
     50                  55                  60

tca tca tca aca caa caa ccg aga gac ctt cat gca gtt gaa act ggg   240
Ser Ser Ser Thr Gln Gln Pro Arg Asp Leu His Ala Val Glu Thr Gly
 65                  70                  75                  80

gtt gac aag aat gag gaa gag gaa gtg cat ctt cag caa gtt atc aat   288
Val Asp Lys Asn Glu Glu Glu Glu Val His Leu Gln Gln Val Ile Asn
                 85                  90                  95

gct gca caa aaa gca ctt ttg ggt tcg aaa aaa gaa gaa aaa agc agt   336
Ala Ala Gln Lys Ala Leu Leu Gly Ser Lys Lys Glu Glu Lys Ser Ser
            100                 105                 110

gat atg tat att ccc aca ccg gac gct tcg agg ata tgg ccc gag gca   384
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Asp Met Tyr Ile Pro Thr Pro Asp Ala Ser Arg Ile Trp Pro Glu Ala
115 120 125

cac aag tat tac aag gat caa aag ttc aag cag cca gag aca tat atc 432
His Lys Tyr Tyr Lys Asp Gln Lys Phe Lys Gln Pro Glu Thr Tyr Ile
130 135 140

aag ttt agt gcg aca gta gag gac aca gtg ggt gtg gag tac aat atg 480
Lys Phe Ser Ala Thr Val Glu Asp Thr Val Gly Val Glu Tyr Asn Met
145 150 155 160

gac gag gta gat gaa aag ttt tat aga gag aca cta tgc aag tac tat 528
Asp Glu Val Asp Glu Lys Phe Tyr Arg Glu Thr Leu Cys Lys Tyr Tyr
165 170 175

ccc aaa aag aaa aac aag tca gat gag aac aat cga aag tgt act gaa 576
Pro Lys Lys Lys Asn Lys Ser Asp Glu Asn Asn Arg Lys Cys Thr Glu
180 185 190

ttg gag ttt gaa aca atc tgt gac aag ttg gaa aag acc att gaa gca 624
Leu Glu Phe Glu Thr Ile Cys Asp Lys Leu Glu Lys Thr Ile Glu Ala
195 200 205

cga caa ccg ttt ttg tct atg gac ccc agc aac att cta tcg tac gag 672
Arg Gln Pro Phe Leu Ser Met Asp Pro Ser Asn Ile Leu Ser Tyr Glu
210 215 220

gag ttg tcg tcg tac att gtg gat cag ttt aaa agt gca gtg aaa aca 720
Glu Leu Ser Ser Tyr Ile Val Asp Gln Phe Lys Ser Ala Val Lys Thr
225 230 235 240

agc aac ccg tat att gtt acc aat ggt ggg aat cta gag tat ata tcg 768
Ser Asn Pro Tyr Ile Val Thr Asn Gly Gly Asn Leu Glu Tyr Ile Ser
245 250 255

acg aca gct tta aaa gag aga ttg tcg aag gaa ata aag tat gaa ccg 816
Thr Thr Ala Leu Lys Glu Arg Leu Ser Lys Glu Ile Lys Tyr Glu Pro
260 265 270

ttt gtt act att ttt gat aag aac caa atg tcc aca agt gcg gtg aga 864
Phe Val Thr Ile Phe Asp Lys Asn Gln Met Ser Thr Ser Ala Val Arg
275 280 285

cct att ccc aaa ttg ttt gag ttg ttc ggc aga cct gtt tat gat cat 912
Pro Ile Pro Lys Leu Phe Glu Leu Phe Gly Arg Pro Val Tyr Asp His
290 295 300

tgg aag gag aga aaa ata gaa aga aag ggc aaa acc atc cag ccc aca 960

```
Trp Lys Glu Arg Lys Ile Glu Arg Lys Gly Lys Thr Ile Gln Pro Thr
305                 310                 315                 320

ctc aaa ttt gag gat cct aac tcg aac gaa aag gaa aac gac aat gac   1008
Leu Lys Phe Glu Asp Pro Asn Ser Asn Glu Lys Glu Asn Asp Asn Asp
                325                 330                 335

cca tat ata tgt ttc aga cga cgt gag ttt agg caa gca aga aag acg   1056
Pro Tyr Ile Cys Phe Arg Arg Arg Glu Phe Arg Gln Ala Arg Lys Thr
            340                 345                 350

aga aga gcc gat aca att ggt gca gag aga ata aga ctg atg caa aag   1104
Arg Arg Ala Asp Thr Ile Gly Ala Glu Arg Ile Arg Leu Met Gln Lys
        355                 360                 365

tcg ttg cac cgc gca cgt gat ttg ata atg agt gtt agt gaa aga gag   1152
Ser Leu His Arg Ala Arg Asp Leu Ile Met Ser Val Ser Glu Arg Glu
    370                 375                 380

atc ctc aaa ctc gac aat ttt caa gca gag cat gaa ttg ttt aaa gcc   1200
Ile Leu Lys Leu Asp Asn Phe Gln Ala Glu His Glu Leu Phe Lys Ala
385                 390                 395                 400

agg tgc gct acc aag gct tgt aag agg gag ctc aat atc aag ggt gac   1248
Arg Cys Ala Thr Lys Ala Cys Lys Arg Glu Leu Asn Ile Lys Gly Asp
                405                 410                 415

gaa tac ttg ttc ttt ccg cat aaa aag aag aaa att gtt cgt act gaa   1296
Glu Tyr Leu Phe Phe Pro His Lys Lys Lys Lys Ile Val Arg Thr Glu
            420                 425                 430

gat gaa gaa agg gag aag aag aga gaa aag aag aag caa gac caa gaa   1344
Asp Glu Glu Arg Glu Lys Lys Arg Glu Lys Lys Lys Gln Asp Gln Glu
        435                 440                 445

ctt gca ctc aag caa caa caa gca cta cag caa cag cag caa caa cca   1392
Leu Ala Leu Lys Gln Gln Gln Ala Leu Gln Gln Gln Gln Gln Gln Pro
    450                 455                 460

cca caa cca cca caa caa gca cca tca aaa caa gat ggt aca tca acg   1440
Pro Gln Pro Pro Gln Gln Ala Pro Ser Lys Gln Asp Gly Thr Ser Thr
465                 470                 475                 480

agc cag cct tat gtc aaa ctc cca ccc gca aaa gtt cca gat atg gat   1488
Ser Gln Pro Tyr Val Lys Leu Pro Pro Ala Lys Val Pro Asp Met Asp
                485                 490                 495

ctt gtt aca gtt tcg ttg gta tta aag gaa aag aac gaa acc atc aaa   1536
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Leu Val Thr Val Ser Leu Val Leu Lys Glu Lys Asn Glu Thr Ile Lys
500 505 510

cgt gct gtg ttg gag aaa ttg cgc aag aga aag gaa cac gac aag gga 1584
Arg Ala Val Leu Glu Lys Leu Arg Lys Arg Lys Glu His Asp Lys Gly
515 520 525

ttt atc aat ttg aca gac gat ccg tat cag cca ttt ttc gat att tca 1632
Phe Ile Asn Leu Thr Asp Asp Pro Tyr Gln Pro Phe Phe Asp Ile Ser
530 535 540

acc aat agg gcc gaa gag ttg agc cat att ccg tat tcg tcg att gcg 1680
Thr Asn Arg Ala Glu Glu Leu Ser His Ile Pro Tyr Ser Ser Ile Ala
545 550 555 560

gcc aca cac tat cac caa ttc aac aca tcg aac tac atg aac gac caa 1728
Ala Thr His Tyr His Gln Phe Asn Thr Ser Asn Tyr Met Asn Asp Gln
565 570 575

ctt aaa aag cta ctt gaa gag aaa aaa cct tta cct ggt gta aaa acg 1776
Leu Lys Lys Leu Leu Glu Glu Lys Lys Pro Leu Pro Gly Val Lys Thr
580 585 590

ttt ttg ggt tct aac ggg gag ttg gta cca tcg aag gca ttt cca cat 1824
Phe Leu Gly Ser Asn Gly Glu Leu Val Pro Ser Lys Ala Phe Pro His
595 600 605

ttg ctg tcg ttg ctt gag gaa aag tat aag gcg aca agt ggg tat att 1872
Leu Leu Ser Leu Leu Glu Glu Lys Tyr Lys Ala Thr Ser Gly Tyr Ile
610 615 620

gaa cga tta ttg caa agc gtg gag acg caa gat ttt agt tca tac acc 1920
Glu Arg Leu Leu Gln Ser Val Glu Thr Gln Asp Phe Ser Ser Tyr Thr
625 630 635 640

aat ggc ttt aaa gat gtt gag cca aaa gaa aca aat gaa cct gtt atg 1968
Asn Gly Phe Lys Asp Val Glu Pro Lys Glu Thr Asn Glu Pro Val Met
645 650 655

gcg ttt ccc cag aga ata cgt cga aga gtg ggc agg gct ggc agg gtt 2016
Ala Phe Pro Gln Arg Ile Arg Arg Arg Val Gly Arg Ala Gly Arg Val
660 665 670

ttt ttg gac cac cag caa gag tac ccg caa ccg aat ttt cag caa gac 2064
Phe Leu Asp His Gln Gln Glu Tyr Pro Gln Pro Asn Phe Gln Gln Asp
675 680 685

aca gat cgt gtg gga ggt atc cca gat gtg tat tgt aaa gag gat gcc 2112

Thr Asp Arg Val Gly Gly Ile Pro Asp Val Tyr Cys Lys Glu Asp Ala
690 695 700

att aaa cga tta cag tca aag tgg aag ttc gat aca gaa tat aaa aca 2160
Ile Lys Arg Leu Gln Ser Lys Trp Lys Phe Asp Thr Glu Tyr Lys Thr
705 710 715 720

act gaa cca ttt agt ttg gat cct tca aag ttg aat ggt att agt cca 2208
Thr Glu Pro Phe Ser Leu Asp Pro Ser Lys Leu Asn Gly Ile Ser Pro
725 730 735

tct acg caa tcg att aga ttt ggg tct atg ttg ttg aat aga aca cgt 2256
Ser Thr Gln Ser Ile Arg Phe Gly Ser Met Leu Leu Asn Arg Thr Arg
740 745 750

aaa tag 2262
Lys

<210> 10
<211> 753
<212> PRT
<213> Candida albicans

<400> 10
Met Ala Ala Ala Pro Pro Pro Pro Ala Lys Asn Gln Gly Lys Ala Lys
1 5 10 15
Gln His Val Thr Gly Ala Arg Phe Arg Gln Arg Lys Ile Ser Val Lys
20 25 30
Gln Pro Leu Thr Ile Tyr Lys Gln Arg Asp Leu Pro Thr Leu Asp Ser
35 40 45
Asn Glu Leu Glu Pro Ser Gln Val His His Leu Asn Ser Asn Ala Ser
50 55 60
Ser Ser Ser Thr Gln Gln Pro Arg Asp Leu His Ala Val Glu Thr Gly
65 70 75 80
Val Asp Lys Asn Glu Glu Glu Glu Val His Leu Gln Gln Val Ile Asn
85 90 95
Ala Ala Gln Lys Ala Leu Leu Gly Ser Lys Lys Glu Glu Lys Ser Ser
100 105 110
Asp Met Tyr Ile Pro Thr Pro Asp Ala Ser Arg Ile Trp Pro Glu Ala
115 120 125
His Lys Tyr Tyr Lys Asp Gln Lys Phe Lys Gln Pro Glu Thr Tyr Ile
130 135 140
Lys Phe Ser Ala Thr Val Glu Asp Thr Val Gly Val Glu Tyr Asn Met
145 150 155 160
Asp Glu Val Asp Glu Lys Phe Tyr Arg Glu Thr Leu Cys Lys Tyr Tyr
165 170 175
Pro Lys Lys Lys Asn Lys Ser Asp Glu Asn Asn Arg Lys Cys Thr Glu

180 185 190

Leu Glu Phe Glu Thr Ile Cys Asp Lys Leu Glu Lys Thr Ile Glu Ala

195 200 205

Arg Gln Pro Phe Leu Ser Met Asp Pro Ser Asn Ile Leu Ser Tyr Glu

210 215 220

Glu Leu Ser Ser Tyr Ile Val Asp Gln Phe Lys Ser Ala Val Lys Thr

225 230 235 240

Ser Asn Pro Tyr Ile Val Thr Asn Gly Gly Asn Leu Glu Tyr Ile Ser

245 250 255

Thr Thr Ala Leu Lys Glu Arg Leu Ser Lys Glu Ile Lys Tyr Glu Pro

260 265 270

Phe Val Thr Ile Phe Asp Lys Asn Gln Met Ser Thr Ser Ala Val Arg

275 280 285

Pro Ile Pro Lys Leu Phe Glu Leu Phe Gly Arg Pro Val Tyr Asp His

290 295 300

Trp Lys Glu Arg Lys Ile Glu Arg Lys Gly Lys Thr Ile Gln Pro Thr

305 310 315 320

Leu Lys Phe Glu Asp Pro Asn Ser Asn Glu Lys Glu Asn Asp Asn Asp

325 330 335

Pro Tyr Ile Cys Phe Arg Arg Arg Glu Phe Arg Gln Ala Arg Lys Thr

340 345 350

Arg Arg Ala Asp Thr Ile Gly Ala Glu Arg Ile Arg Leu Met Gln Lys

355 360 365

Ser Leu His Arg Ala Arg Asp Leu Ile Met Ser Val Ser Glu Arg Glu

370 375 380

Ile Leu Lys Leu Asp Asn Phe Gln Ala Glu His Glu Leu Phe Lys Ala

385 390 395 400

Arg Cys Ala Thr Lys Ala Cys Lys Arg Glu Leu Asn Ile Lys Gly Asp

405 410 415

Glu Tyr Leu Phe Phe Pro His Lys Lys Lys Lys Ile Val Arg Thr Glu

420 425 430

Asp Glu Glu Arg Glu Lys Lys Arg Glu Lys Lys Lys Gln Asp Gln Glu

435 440 445

Leu Ala Leu Lys Gln Gln Gln Ala Leu Gln Gln Gln Gln Gln Gln Pro

450 455 460

Pro Gln Pro Pro Gln Gln Ala Pro Ser Lys Gln Asp Gly Thr Ser Thr

465 470 475 480

Ser Gln Pro Tyr Val Lys Leu Pro Pro Ala Lys Val Pro Asp Met Asp

485 490 495

Leu Val Thr Val Ser Leu Val Leu Lys Glu Lys Asn Glu Thr Ile Lys

500 505 510

Arg Ala Val Leu Glu Lys Leu Arg Lys Arg Lys Glu His Asp Lys Gly

515 520 525

Phe Ile Asn Leu Thr Asp Asp Pro Tyr Gln Pro Phe Phe Asp Ile Ser

530 535 540

Thr Asn Arg Ala Glu Glu Leu Ser His Ile Pro Tyr Ser Ser Ile Ala

545 550 555 560

Ala Thr His Tyr His Gln Phe Asn Thr Ser Asn Tyr Met Asn Asp Gln

565 570 575
Leu Lys Lys Leu Leu Glu Glu Lys Lys Pro Leu Pro Gly Val Lys Thr
580 585 590
Phe Leu Gly Ser Asn Gly Glu Leu Val Pro Ser Lys Ala Phe Pro His
595 600 605
Leu Leu Ser Leu Leu Glu Glu Lys Tyr Lys Ala Thr Ser Gly Tyr Ile
610 615 620
Glu Arg Leu Leu Gln Ser Val Glu Thr Gln Asp Phe Ser Ser Tyr Thr
625 630 635 640
Asn Gly Phe Lys Asp Val Glu Pro Lys Glu Thr Asn Glu Pro Val Met
645 650 655
Ala Phe Pro Gln Arg Ile Arg Arg Arg Val Gly Arg Ala Gly Arg Val
660 665 670
Phe Leu Asp His Gln Gln Glu Tyr Pro Gln Pro Asn Phe Gln Gln Asp
675 680 685
Thr Asp Arg Val Gly Gly Ile Pro Asp Val Tyr Cys Lys Glu Asp Ala
690 695 700
Ile Lys Arg Leu Gln Ser Lys Trp Lys Phe Asp Thr Glu Tyr Lys Thr
705 710 715 720
Thr Glu Pro Phe Ser Leu Asp Pro Ser Lys Leu Asn Gly Ile Ser Pro
725 730 735
Ser Thr Gln Ser Ile Arg Phe Gly Ser Met Leu Leu Asn Arg Thr Arg
740 745 750
Lys

<210> 11
<211> 447
<212> DNA
<213> Candida albicans

<220>
<221> CDS
<222> (1)..(447)

<400> 11
atg tca gat ata gat ata gat aat gta tta aat tta gaa gaa gaa caa 48
Met Ser Asp Ile Asp Ile Asp Asn Val Leu Asn Leu Glu Glu Glu Gln
1 5 10 15

tat gaa tta gga ttt aaa gaa ggt caa ata caa gga aca aaa gat caa 96
Tyr Glu Leu Gly Phe Lys Glu Gly Gln Ile Gln Gly Thr Lys Asp Gln
20 25 30

tat tta gaa gga aaa gaa tat ggt tat caa act gga ttt caa cga ttt 144
Tyr Leu Glu Gly Lys Glu Tyr Gly Tyr Gln Thr Gly Phe Gln Arg Phe
35 40 45

tta atc att ggt tat att caa gaa tta atg aaa ttt tgg tta tcc cat 192
Leu Ile Ile Gly Tyr Ile Gln Glu Leu Met Lys Phe Trp Leu Ser His
50 55 60

ata gat caa tat aat aac tct tct tca ctt cgg aat cat ttg aat aat 240
Ile Asp Gln Tyr Asn Asn Ser Ser Ser Leu Arg Asn His Leu Asn Asn
65 70 75 80

ttg gaa gat att atg gca caa att tct ata acg aat gga gat aaa gaa 288
Leu Glu Asp Ile Met Ala Gln Ile Ser Ile Thr Asn Gly Asp Lys Glu
85 90 95

gtt gaa gat tat gaa aaa aat att aaa aag gca aga aat aaa tta aga 336
Val Glu Asp Tyr Glu Lys Asn Ile Lys Lys Ala Arg Asn Lys Leu Arg
100 105 110

gtg ata gct agt ata act aaa gaa act tgg aaa att gat tca ttg gat 384
Val Ile Ala Ser Ile Thr Lys Glu Thr Trp Lys Ile Asp Ser Leu Asp
115 120 125

aat ttg gtg aaa gaa gta ggt gga act tta caa gtt agt gaa aac ccc 432
Asn Leu Val Lys Glu Val Gly Gly Thr Leu Gln Val Ser Glu Asn Pro
130 135 140

gat gat atg tgg tga 447
Asp Asp Met Trp
145

<210> 12
<211> 148
<212> PRT
<213> Candida albicans

<400> 12
Met Ser Asp Ile Asp Ile Asp Asn Val Leu Asn Leu Glu Glu Glu Gln
1 5 10 15
Tyr Glu Leu Gly Phe Lys Glu Gly Gln Ile Gln Gly Thr Lys Asp Gln
20 25 30
Tyr Leu Glu Gly Lys Glu Tyr Gly Tyr Gln Thr Gly Phe Gln Arg Phe
35 40 45
Leu Ile Ile Gly Tyr Ile Gln Glu Leu Met Lys Phe Trp Leu Ser His
50 55 60
Ile Asp Gln Tyr Asn Asn Ser Ser Ser Leu Arg Asn His Leu Asn Asn
65 70 75 80
Leu Glu Asp Ile Met Ala Gln Ile Ser Ile Thr Asn Gly Asp Lys Glu
85 90 95

Val Glu Asp Tyr Glu Lys Asn Ile Lys Lys Ala Arg Asn Lys Leu Arg
100 105 110
Val Ile Ala Ser Ile Thr Lys Glu Thr Trp Lys Ile Asp Ser Leu Asp
115 120 125
Asn Leu Val Lys Glu Val Gly Gly Thr Leu Gln Val Ser Glu Asn Pro
130 135 140
Asp Asp Met Trp
145

<210> 13
<211> 966
<212> DNA
<213> Candida albicans

<220>
<221> CDS
<222> (1)..(966)

<400> 13
atg ggt aaa aga aga gta gat gaa gaa tct gat tca gat att gat gtt 48
Met Gly Lys Arg Arg Val Asp Glu Glu Ser Asp Ser Asp Ile Asp Val
1 5 10 15

agt tca acc gat tca gaa act gaa tta gaa agc aca caa caa caa caa 96
Ser Ser Thr Asp Ser Glu Thr Glu Leu Glu Ser Thr Gln Gln Gln Gln
20 25 30

caa caa caa gaa ggt gct act aca att caa gaa act gtt gat gtt gat 144
Gln Gln Gln Glu Gly Ala Thr Thr Ile Gln Glu Thr Val Asp Val Asp
35 40 45

ttt gat ttt ttt gat tta aat cct caa att gat ttc cat gct act aag 192
Phe Asp Phe Phe Asp Leu Asn Pro Gln Ile Asp Phe His Ala Thr Lys
50 55 60

aat ttt tta aga caa tta ttt ggt gat gat aat gga gaa ttt aat tta 240
Asn Phe Leu Arg Gln Leu Phe Gly Asp Asp Asn Gly Glu Phe Asn Leu
65 70 75 80

agt gaa ata gcc gat tta att tta cga gaa aat tcc gtg ggg aca tca 288
Ser Glu Ile Ala Asp Leu Ile Leu Arg Glu Asn Ser Val Gly Thr Ser
85 90 95

att aaa act gaa gga atg gaa agt gat cca ttt gca att tta agt gta 336
Ile Lys Thr Glu Gly Met Glu Ser Asp Pro Phe Ala Ile Leu Ser Val
100 105 110

att aat tta act aat aat tta aat gtg gcc gtg att aaa caa ttg att 384
Ile Asn Leu Thr Asn Asn Leu Asn Val Ala Val Ile Lys Gln Leu Ile
115 120 125

gaa tat att tca aat aaa acc aaa tct aaa act gaa ttc aat att att 432
Glu Tyr Ile Ser Asn Lys Thr Lys Ser Lys Thr Glu Phe Asn Ile Ile
130 135 140

ttg aaa aaa ttg tta acc aat cag aac gat act act aga gat agg aaa 480
Leu Lys Lys Leu Leu Thr Asn Gln Asn Asp Thr Thr Arg Asp Arg Lys
145 150 155 160

ttt aaa act gga tta ata att agt gaa aga ttt ata aat atg cca gtt 528
Phe Lys Thr Gly Leu Ile Ile Ser Glu Arg Phe Ile Asn Met Pro Val
165 170 175

gaa gtg att cca cca atg tat aaa atg ctt tta caa gaa atg gaa aaa 576
Glu Val Ile Pro Pro Met Tyr Lys Met Leu Leu Gln Glu Met Glu Lys
180 185 190

gct gaa gat gct cat gaa aat tat gaa ttt gat tat ttt tta att ata 624
Ala Glu Asp Ala His Glu Asn Tyr Glu Phe Asp Tyr Phe Leu Ile Ile
195 200 205

tca aga gtt tat caa tta gtt gat cca gtg gaa aga gaa gat gaa gat 672
Ser Arg Val Tyr Gln Leu Val Asp Pro Val Glu Arg Glu Asp Glu Asp
210 215 220

cac gaa aaa gaa tcc aat cgt aaa aag aag aac aag aat aag aag aag 720
His Glu Lys Glu Ser Asn Arg Lys Lys Lys Asn Lys Asn Lys Lys Lys
225 230 235 240

aaa ttg gct aat aat gaa cca aaa cca ata gaa atg gat tat ttc cat 768
Lys Leu Ala Asn Asn Glu Pro Lys Pro Ile Glu Met Asp Tyr Phe His
245 250 255

ctt gaa gat caa att ttg gaa tca aat act caa ttt aaa gga ata ttt 816
Leu Glu Asp Gln Ile Leu Glu Ser Asn Thr Gln Phe Lys Gly Ile Phe
260 265 270

gaa tat aat aat gaa aat aaa caa gaa aca gat tca aga aga gta ttt 864
Glu Tyr Asn Asn Glu Asn Lys Gln Glu Thr Asp Ser Arg Arg Val Phe
275 280 285

act gaa tat ggt att gat cct aaa tta agt tta atc tta att gat aaa 912
Thr Glu Tyr Gly Ile Asp Pro Lys Leu Ser Leu Ile Leu Ile Asp Lys
290 295 300

gat aat tta gct aaa tca gtc att gaa atg gaa caa caa ttc cca cct 960
Asp Asn Leu Ala Lys Ser Val Ile Glu Met Glu Gln Gln Phe Pro Pro
305 310 315 320

cca taa 966
Pro

<210> 14
<211> 321
<212> PRT
<213> Candida albicans

<400> 14
Met Gly Lys Arg Arg Val Asp Glu Glu Ser Asp Ser Asp Ile Asp Val
1 5 10 15
Ser Ser Thr Asp Ser Glu Thr Glu Leu Glu Ser Thr Gln Gln Gln Gln
20 25 30
Gln Gln Gln Glu Gly Ala Thr Thr Ile Gln Glu Thr Val Asp Val Asp
35 40 45
Phe Asp Phe Phe Asp Leu Asn Pro Gln Ile Asp Phe His Ala Thr Lys
50 55 60
Asn Phe Leu Arg Gln Leu Phe Gly Asp Asp Asn Gly Glu Phe Asn Leu
65 70 75 80
Ser Glu Ile Ala Asp Leu Ile Leu Arg Glu Asn Ser Val Gly Thr Ser
85 90 95
Ile Lys Thr Glu Gly Met Glu Ser Asp Pro Phe Ala Ile Leu Ser Val
100 105 110
Ile Asn Leu Thr Asn Asn Leu Asn Val Ala Val Ile Lys Gln Leu Ile
115 120 125
Glu Tyr Ile Ser Asn Lys Thr Lys Ser Lys Thr Glu Phe Asn Ile Ile
130 135 140
Leu Lys Lys Leu Leu Thr Asn Gln Asn Asp Thr Thr Arg Asp Arg Lys
145 150 155 160
Phe Lys Thr Gly Leu Ile Ile Ser Glu Arg Phe Ile Asn Met Pro Val
165 170 175
Glu Val Ile Pro Pro Met Tyr Lys Met Leu Leu Gln Glu Met Glu Lys
180 185 190
Ala Glu Asp Ala His Glu Asn Tyr Glu Phe Asp Tyr Phe Leu Ile Ile
195 200 205
Ser Arg Val Tyr Gln Leu Val Asp Pro Val Glu Arg Glu Asp Glu Asp
210 215 220
His Glu Lys Glu Ser Asn Arg Lys Lys Lys Asn Lys Asn Lys Lys Lys
225 230 235 240
Lys Leu Ala Asn Asn Glu Pro Lys Pro Ile Glu Met Asp Tyr Phe His
245 250 255
Leu Glu Asp Gln Ile Leu Glu Ser Asn Thr Gln Phe Lys Gly Ile Phe

260 265 270
Glu Tyr Asn Asn Glu Asn Lys Gln Glu Thr Asp Ser Arg Arg Val Phe
275 280 285
Thr Glu Tyr Gly Ile Asp Pro Lys Leu Ser Leu Ile Leu Ile Asp Lys
290 295 300
Asp Asn Leu Ala Lys Ser Val Ile Glu Met Glu Gln Gln Phe Pro Pro
305 310 315 320
Pro

<210> 15
<211> 320
<212> DNA
<213> Candida albicans

<400> 15
caatttattc atggtccgtt ctggaaattg atttttggta aaactgctaa tgaattagaa 60
aaatcgcaag atttgcccaa tgaatatatg attgtggaga atgtgccatt attaaataga 120
tttattagta tacctaagga gtatggcgac ttaaattgtt cagcatttgt tgcgggtata 180
attgagggag cacttgataa tagtggattc aatgccgatg ttacagcaca cacggtcgct 240
acagatgcaa atccattaag aacagtattt ttgatcaagt ttgacgattc tgttttaatt 300
agagagagtt tgagatttgg 320

<210> 16
<211> 295
<212> DNA
<213> Candida albicans

<400> 16
gttcatgttt ggtgactcag agcgtctcaa ctatattgtt cgattataca tacgaactcg 60
attgagtaag ttgaataaat ttactatttt ttacatcaat gaaagcagtc aaaatgataa 120
tttattgtcc aaagaggaaa gagattatat acacaaatat ttccagattt tgactcaatt 180
atataacaac tgtttcctca aaaaactacc acaaatgttg acctatttgg atgacaccag 240
tggtggacaa tcaatgatcg ttgagccaga tttagaccag cctgtgttta tcaaa 295

<210> 17
<211> 392
<212> DNA
<213> Candida albicans

<400> 17
atctctgata tgagatttgg ctttaaaggc gatttaattg aattggctcc agtgggagat 60
gcaccaaaag atagttcatc cgacatacgt actcatatgg gactccatca tcattcggag 120
accccacata tggcaggtta tacattgggt gagttggccc atttagccag atcgacttta 180
gctggacaaa gatgcttgag cattcaaaca ttagggagaa tcttccataa attgggatta 240

cataaataca gtatactacc aaaccagctc aatgatcaga gttttacaga tgaatcaaaa 300
ctatcacttg actttgaaga tagatgtggg acttgataga ccaattacga atcattgaaa 360
caataacaga ggcagctgat ggaaaaaaga cc 392

<210> 18
<211> 335
<212> DNA
<213> Candida albicans

<400> 18
attcccacac cggacgcttc gaggatatgg cccgaggcac acaagtatta caaggatcaa 60
aagttcaagc agccagagac atatatcaag tttagtgcga cagtagagga cacagtgggt 120
gtggagtaca atatggacga ggtagatgaa aagttttata gagagacact atgcaagtac 180
tatcccaaaa agaaaaacaa gtcagatgag aacaatcgaa agtgtactga attggagttt 240
gaaacaatct gtgacaagtt ggaaaagacc attgaagcac gacaaccgtt tttgtctatg 300
gaccccagca acattctatc gtacgaggag ttgtc 335

<210> 19
<211> 326
<212> DNA
<213> Candida albicans

<400> 19
agatatagat aatgtattaa atttagaaga agatcaatat gaattaggat ttaaagaagg 60
tcaaatacaa ggaacaaaag atcaatattt agaaggaaaa gaatatggtt atcaaactgg 120
atttcaacga tttttaatca ttggttatat tcaagaatta atgaaatttt ggttatccca 180
tatagatcaa tataataact cttcttcact tcggaatcat ttgaataatt tggaagatat 240
tatggcacaa atttctataa cgaatggaga taaagaagtt gaagattatg aaaaaaatat 300
taaaaaggca agaaataaat taagag 326

<210> 20
<211> 374
<212> DNA
<213> Candida albicans

<400> 20
cctcaaattg atttccatgc tactaagaat ttttaagaca ttatttggtg atgataatgg 60
agaatttaat ttaagtgaaa tagccgattt aattttacga gaaaattccg tggggacatc 120
aattaaaact gaaggaatgg aaagtgatcc atttgcaatt ttaagtgtaa ttaatttaac 180
taataattta aatgtggccg tgattaaaca attgattgaa tatattttaa ataaaaccaa 240
atctaaaact gaattcaata ttattttgaa aaaattgtta accaatcaga acgatactac 300
tagagatagg aaatttaaaa ctggattaat aattagtgaa agatttataa atatgccagt 360
tgaagtgatt ccac 374

<210> 21
<211> 35
<212> DNA
<213> Candida albicans

<220>
<221> modified_base
<222> (18)
<223> n=a or g or c or t

<400> 21
caatttattc atgttcgnat ctggaaattg atttt 35

<210> 22
<211> 29
<212> DNA
<213> Candida albicans

<400> 22
ccaaatctca aactctctct aattaaaac 29

<210> 23
<211> 38
<212> DNA
<213> Candida albicans

<400> 23
gttcatgttt ggtgactcag agcgtctcaa ctatattg 38

<210> 24
<211> 33
<212> DNA
<213> Candida albicans

<400> 24
tttgataaac acaggctggt ctaaatctgg ctc 33

<210> 25
<211> 32
<212> DNA
<213> Candida albicans

<400> 25
atctctgata tgagatttgg ctttaaaggc ga 32

<210> 26
<211> 32
<212> DNA
<213> Candida albicans

<400> 26
ggtctttttt ccatcagctg cctctgttat tg 32

<210> 27
<211> 20
<212> DNA
<213> Candida albicans

<400> 27
attcccacac cggacgcttc 20

<210> 28
<211> 20
<212> DNA
<213> Candida albicans

<400> 28
gacaactcct cgtacgatag 20

<210> 29
<211> 20
<212> DNA
<213> Candida albicans

<400> 29
agataatgta ttaaatttag 20

<210> 30
<211> 20
<212> DNA
<213> Candida albicans

<400> 30
ctcttaattt atttcttgcc 20

<210> 31

<211> 20
<212> DNA
<213> Candida albicans

<400> 31
cctcaaattg atttccatgc 20

<210> 32
<211> 20
<212> DNA
<213> Candida albicans

<400> 32
gtggaatcac ttcaactggc 20